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JULY 1934

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, July 10, 1925, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of Oct. 3, 1917, authorized July 29, 1920.

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ARCHIVES OF SURGERY

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AVERTIN (TRIBROMETHANOL) ANESTHESIA IN NORMAL PERSONS

ERNEST E. ARNHEIM, M.D.
AND
LESTER R. TUCHMAN, M.D.
NEW YORK

Although the literature on avertin (tribromethanol) rectal anesthesia has become voluminous since the production of the chemical compound tribromethanol by Willstätter and Duisberg, in 1923, there are only a few investigations on the effects in normal persons of the drug administered alone, in the dosage used in basal anesthesia. Before we were willing to employ avertin anesthesia on a large scale in hospital practice, we deemed it advisable to investigate the effects of the drug in normal persons. The numerous reports recorded present either experiments on animals or observations on persons with such complicating factors as operation, auxiliary medication and supplementary anesthesia.

METHOD

We studied avertin anesthesia in fifteen normal people with a view to obtaining information on the uncomplicated effects of the drug. We made observations on the following: age, sex, weight, dosage, constitution, pulse, temperature, respiratory rate and amplitude, condition of the reflexes, state of consciousness, presence of cyanosis and emesis, arterial and venous blood pressure, basal metabolism, complete blood chemistry, hematology and urinary findings. The observations were recorded: (1) in repose, immediately before the administration of the drug; (2) one hour after its introduction, when the anesthesia was at its height, and (3) four hours after its introduction, toward the end of the anesthesia. No auxiliary medication was given. In the studies avertin fluid was used, 1 cc. of fluid containing 1 Gm. of tribromethyl-alcohol and 0.5 Gm. of amylene hydrate. Solutions of avertin fluid were prepared according to the manufacturer's instructions in a 2.5 per cent solution in distilled water at a moderate temperature of from 95 to 104 F. (35 to 40 C.). The patients were healthy persons admitted to the surgical service for relatively minor operations—for the most part, inguinal hernioplasties. The operations were performed after the studies on avertin were completed. Little additional anesthesia was required for the operations, and there were no untoward effects.

OBSERVATIONS

Age, Sex, Dosage and Constitution.—The first table gives the age, sex, weight and dosage of avertin and a few remarks on the complexion

From the surgical service of Dr. Harold Neuhof and from the laboratories of the Mount Sinai Hospital.

and nervous make-up of the fifteen patients studied. There were ten men and five women. The youngest patient was 17 years of age, and the oldest 52. The weight varied between 105 and 160 pounds (48 and 73 Kg.). The average dosage of avertin fluid was 6.2 cc. One half of the patients were considered to be of a normal nervous make-up, one third excitable and the remainder phlegmatic.

Pulse, Temperature, Respiration, Reflexes and Untoward Symptoms.—Table 2 gives the pulse rate, temperature, respiratory rate and amplitude, condition of reflexes, state of consciousness and presence of untoward symptoms.

The average pulse rate before anesthesia was 73, the variations being between a low rate of 56 and a high rate of 96. After one hour of

TABLE 1.—*Age, Sex, Weight, Dosage and Constitution*

Case	Age	Sex	Weight, Pounds	Dosage, Mg. per Kg. Body Weight	Amount of Avertin Fluid, Cc.	Complexion	Nervous Make-Up
1	52	M	148	100	6.8	Light	Phlegmatic
2	46	M	144	100	6.6	Light	Phlegmatic
3	43	M	160	100	7.3	Light	Excitable
4	39	M	105	100	4.8	Dark	Excitable
5	17	M	140	100	6.4	Dark	Normal
6	22	M	153	100	7.0	Dark	Normal
7	41	M	119	100	5.4	Dark	Excitable
8	26	M	129	100	5.8	Negro	Normal
9	48	M	159	100	7.2	Dark	Normal
10	17	M	120	100	5.4	Negro	Normal
11	46	F	160	100	7.0	Dark	Normal
12	37	F	130	100	5.8	Dark	Excitable
13	23	F	113	100	5.1	Light	Normal
14	48	F	133	100	6.0	Dark	Normal
15	30	F	140	100	6.3	Dark	Excitable

anesthesia the average pulse rate had risen to 89, with a low rate of 68 and a high rate of 110. In only two patients was there a fall in pulse rate at the end of one hour, and both of these were excitable people with pulse rates of 92 and 96 before anesthesia. At the end of four hours of anesthesia the average pulse rate was 83, an increase from the preliminary rate but a fall from the rate observed at the end of one hour.

The average rectal temperature before anesthesia was 99.1 F. At the end of one hour of anesthesia the temperature in every instance fell, the average temperature being 97.8 F. and the greatest fall 2 F. After four hours the temperatures in every case were still lower than the preliminary temperatures, but they tended to return to their original figures, the average temperature being 98 F.

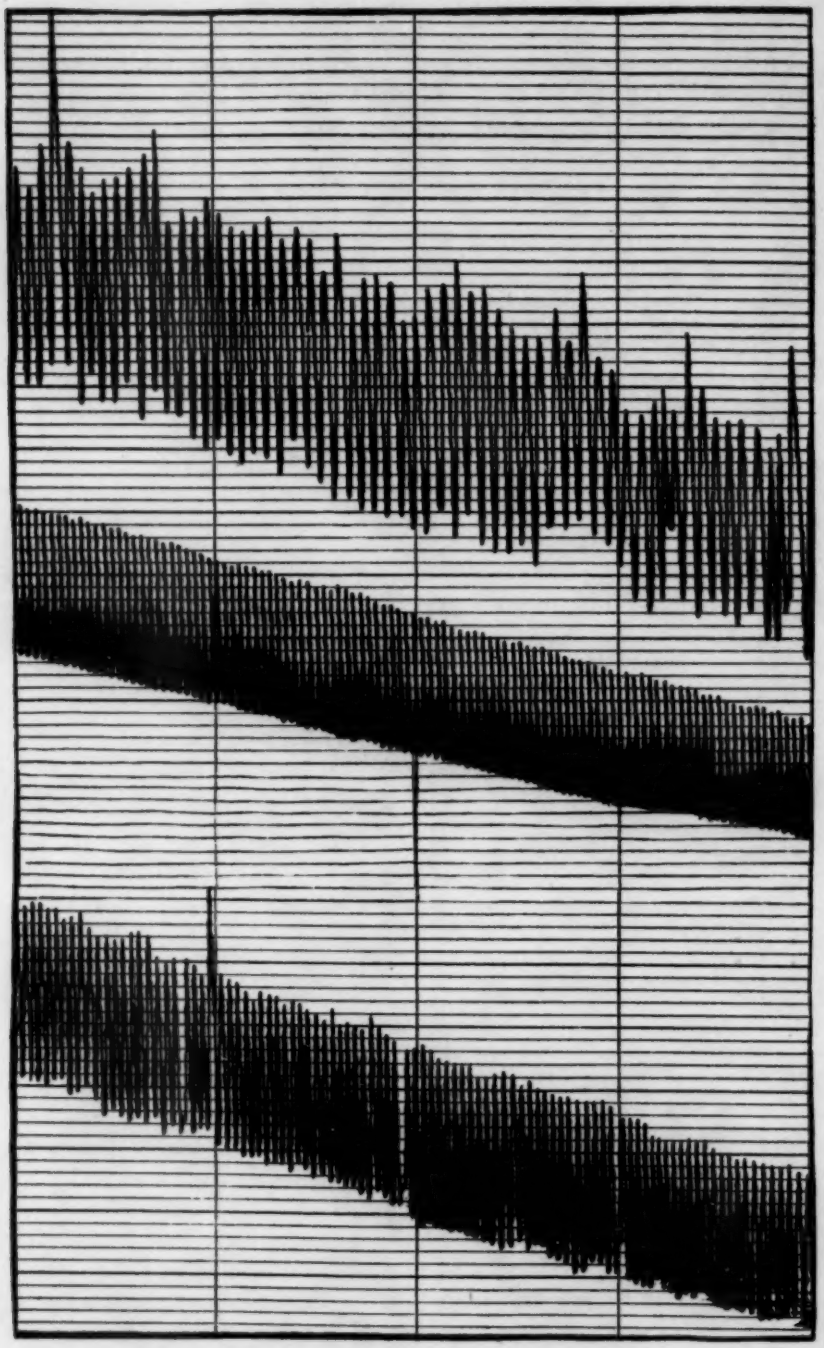
The preliminary respiratory rate varied between 12 and 26, with an average of 16. After one hour of anesthesia the respiratory rate varied between 16 and 26, with an average of 22. There was a rise in respira-

tory rate in every case except one, in which instance the preliminary rate was 26, the highest recorded. At the end of four hours of anesthesia the average respiratory rate was 20.

TABLE 2.—*Pulse, Temperature, Respiration, Reflexes and Untoward Symptoms*

Case	Time	Pulse Rate	Temperature	Respiratory Rate	Respiratory Amplitude, Mm.	Condition of Reflexes, Corneal and Knee Jerk	State of Consciousness	Untoward Symptoms
1	Before anesthesia....	74	98.2	12	38	Present ++	Normal	
	1 hour of anesthesia.	110	96.8	16	Shallow	Absent 0	Absent	
	4 hours of anesthesia	72	97.0	17	31	Present +	Awake	Mucus
2	Before anesthesia....	60	98.0	13	35	Present +	Normal	Slight cyanosis
	1 hour of anesthesia.	96	97.2	19	25	Absent 0	Absent	Mucus
	4 hours of anesthesia	94	97.4	24	..	Present +	Asleep	Emesis
3	Before anesthesia....	64	99.0	17	27	Present ++	Normal	
	1 hour of anesthesia.	100	98.0	25	17	Absent 0	Absent	
	4 hours of anesthesia	80	97.8	22	..	Present ++	Awake	
4	Before anesthesia....	74	99.0	16	Deep	Present ++	Normal	Slight cyanosis
	1 hour of anesthesia.	102	97.8	24	Shallow	Absent 0	Awake at end of 2 hours	Excitable and difficult to control at the end of 2 hours
5	Before anesthesia....	60	99.2	17	39	Present ++	Normal	
	1 hour of anesthesia.	88	97.2	22	18	Absent 0	Absent	
	4 hours of anesthesia	68	97.4	24	Shallow	Absent ++	Asleep	
6	Before anesthesia....	60	98.6	14	40	Present ++	Normal	Mucus
	1 hour of anesthesia.	90	97.2	20	29	Absent 0	Absent	
	4 hours of anesthesia	96	98.0	20	34	Present +	Awake	
7	Before anesthesia....	88	99.6	12	36	Present ++	Normal	
	1 hour of anesthesia.	96	97.8	16	22	Absent 0	Absent	
	4 hours of anesthesia	90	97.8	13	40	Present +	Awake	
8	Before anesthesia....	60	98.8	20	34	Present ++	Normal	
	1 hour of anesthesia.	68	97.2	20	26	Absent 0	Absent	
	4 hours of anesthesia	52	97.6	18	25	Present +	Asleep	
9	Before anesthesia....	68	98.6	15	42	Present +	Normal	
	1 hour of anesthesia.	74	98.0	24	29	Absent 0	Absent	
	4 hours of anesthesia	72	98.2	20	33	Present 0	Awake	
10	Before anesthesia....	56	99.2	20	38	Present +	Normal	
	1 hour of anesthesia.	78	97.2	20	27	Absent 0	Absent	
	4 hours of anesthesia	68	97.8	18	36	Present 0	Asleep	
11	Before anesthesia....	76	99.2	14	40	Present ++	Normal	
	1 hour of anesthesia.	84	98.2	24	24	Absent 0	Absent	Mucus
	4 hours of anesthesia	100	98.6	20	30	Present 0	Awake	Emesis
12	Before anesthesia....	92	99.8	26	25	Present +	Normal	Mucus
	1 hour of anesthesia.	76	98.4	22	27	Absent 0	Absent	
	4 hours of anesthesia	70	98.8	24	26	Present +	Awake	Emesis
13	Before anesthesia....	84	100.2	15	34	Present ++	Normal	
	1 hour of anesthesia.	84	99.0	26	23	Absent 0	Absent	
	4 hours of anesthesia	100	98.8	24	25	Present ++	Awake	
14	Before anesthesia....	86	99.0	17	32	Present ++	Normal	
	1 hour of anesthesia.	104	98.6	26	23	Absent 0	Absent	
	4 hours of anesthesia	122	98.8	18	..	Present ++	Asleep	
15	Before anesthesia....	96	99.8	17	34	Present ++	Normal	
	1 hour of anesthesia.	88	98.0	26	32	Absent 0	Absent	
	4 hours of anesthesia	82	98.0	24	..	Present ++	Asleep	
Averages								
	Before anesthesia....	73	99.1	16	35			
	1 hour of anesthesia.	89	97.8	22	25			
	4 hours of anesthesia	83	98.0	20	31			

The respiratory rate and amplitude were taken from the graphs of the basal metabolic readings. A typical graph is given. The figures for respiratory amplitude in table 2 are measurements in millimeters of the height of the respiratory curve in the basal metabolic graphs. In this way we were able to use exact measurements instead of such terms



Typical graph for the basal metabolic reading, showing respiratory rate and amplitude: Upper curve, before anesthesia; middle curve, after one hour of anesthesia, and lower curve, after four hours of anesthesia.

as deep and shallow. The average amplitude of respiration before anesthesia was 35 mm.; after one hour, 25 mm., and after four hours, 31 mm., representing a decrease at the end of one hour which was not quite made up at the end of four hours. Thus it can be seen that with an increase in the respiratory rate there is a decrease in the respiratory amplitude.

In these studies purely mechanical faults, such as a falling back of the tongue and jaw, were eliminated. Many of the reports in the literature of slow, shallow respirations were due to the unfavorable combination of avertin with the supporting narcotic.

In all of the cases corneal reflexes and knee jerks were absent at the end of one hour of anesthesia but in most of the cases had returned at the end of four hours. In studying the cases it was noted that the conjunctival and corneal reflexes disappeared first. Then a loss of muscular tension occurred and lastly a disappearance of tendon and skin reflexes. The pupils were at first narrow, and they dilated when struck by light. Then a state of contraction without reaction to light followed. The pupils next gradually dilated with a slow reaction to light, finally returning to their normal status. Pharyngeal and tracheal reflexes, as illustrated by inducing swallowing and cough, were preserved late.

At the end of four hours of anesthesia, nine patients were awake. The remaining patients, with the exception of one, had recovered from the primary anesthesia and appeared to be sleeping naturally. In one case the patient was excitable and difficult to control at the end of two hours.

Slight cyanosis was noted in two cases. In five cases there was an accumulation of a moderate amount of mucus in the pharynx. Vomiting in slight degree occurred in three cases. The uniform absence of sweating was of interest, in contrast to the usual profuse perspiration in inhalation and spinal anesthesia.

Arterial and Venous Blood Pressure.—Observations on the arterial and venous blood pressure are shown in table 3. In thirteen cases there was a drop in systolic blood pressure; in one case, a slight rise, and in one case, no change. The average systolic pressure before anesthesia was 113 mm. of mercury, with a high level of 140 and a low level of 96. At the end of one hour the average systolic pressure was 89 mm., with a high level of 108 and a low level of 68. At the end of four hours the average systolic pressure was 102 mm. with a high level of 118 and a low level of 70. The average fall in systolic pressure was 24 mm. for the determination at the end of one hour of anesthesia and 11 mm. for that at the end of four hours.

There were a drop in diastolic blood pressure in eleven cases, a rise in two cases and no change in two cases. The average diastolic pressure

before anesthesia was 71 mm. with a high level of 96 and a low level of 58. At the end of one hour the average diastolic pressure was 63 mm., with a high level of 90 and a low level of 50. At the end of four hours the average diastolic pressure was 66 mm., with a high level of 90 and

TABLE 3.—*Arterial and Venous Blood Pressure*

Case	Time	Systolic Pressure, Mm. Hg*	Diastolic Pressure, Mm. Hg*	Pulse Pressure, Mm. Hg*	Venous Pressure, Cm. H_2O
1	Before anesthesia.....	108	78	30	6.5
	1 hour after anesthesia...	108	90	18	9.0
	4 hours after anesthesia..	108	80	28	9.0
2	Before anesthesia.....	102	76	26	5.0
	1 hour after anesthesia...	88	60	28	8.0
	4 hours after anesthesia..	80	50	30	5.0
3	Before anesthesia.....	122	80	42	5.5
	1 hour after anesthesia...	80	60	20	8.0
	4 hours after anesthesia..	110	68	42	3.0
4	Before anesthesia.....	106	60	46	8.5
	1 hour after anesthesia...	94	60	34	10.0 (strained)
	4 hours after anesthesia..	..	..	..	...
5	Before anesthesia.....	98	70	28	5.0
	1 hour after anesthesia...	100	70	30	10.0 (strained)
	4 hours after anesthesia..	104	70	34	...
6	Before anesthesia.....	96	60	36	9.0
	1 hour after anesthesia...	88	64	24	8.0
	4 hours after anesthesia..	110	76	34	8.0
7	Before anesthesia.....	120	60	60	3.0
	1 hour after anesthesia...	100	58	42	4.0
	4 hours after anesthesia..	110	60	50	...
8	Before anesthesia.....	110	70	40	8.0
	1 hour after anesthesia...	86	60	26	12.0 (strained)
	4 hours after anesthesia..	84	60	24	...
9	Before anesthesia.....	140	96	44	3.0
	1 hour after anesthesia...	68	54	14	4.0
	4 hours after anesthesia..	112	90	22	...
10	Before anesthesia.....	104	64	40	5.0
	1 hour after anesthesia...	84	58	26	8.0
	4 hours after anesthesia..	70	50	20	...
11	Before anesthesia.....	114	70	44	4.0
	1 hour after anesthesia...	88	54	34	4.0
	4 hours after anesthesia..	110	70	40	4.0
12	Before anesthesia.....	136	80	56	5.0
	1 hour after anesthesia...	100	70	30	3.5
	4 hours after anesthesia..	118	70	48	5.0
13	Before anesthesia.....	96	58	38	3.0
	1 hour after anesthesia...	80	58	22	4.5
	4 hours after anesthesia..	94	50	44	3.0
14	Before anesthesia.....	122	70	52	3.5
	1 hour after anesthesia...	100	60	40	3.5
	4 hours after anesthesia..	114	64	50	...
15	Before anesthesia.....	116	68	48	8.0
	1 hour after anesthesia...	78	64	14	7.0
	4 hours after anesthesia..	106	70	36	...
Averages	Before anesthesia.....	113	71	42	5.5
	1 hour after anesthesia...	89	63	26	6.9
	4 hours after anesthesia..	102	66	36	5.3

* Mercury.

a low level of 50. The average fall in diastolic pressure was 8 mm. at the end of one hour and 5 mm. at the end of four hours.

It might be noted that the greatest drop in blood pressure (72 mm., systolic pressure; 42, diastolic pressure) was in case 9, which showed the highest blood pressure before operation.

The pulse pressure dropped in thirteen cases and rose in two. The average pulse pressure before anesthesia was 42 mm., with a high value of 60 and a low value of 26. At the end of one hour of anesthesia the average pulse pressure was 26, with a high value of 42 and a low value of 14. At the end of four hours the average pulse pressure was 36, with a high value of 50 and a low value of 20. The average fall in pulse pressure was 20 mm. in one hour and 6 mm. in four hours.

According to other observers (Anschütz, Specht and Tiemann,[1] Ransom [2] and Taylor and Lund [3]) the blood pressure almost uniformly drops, but the pulse pressure is changed only slightly. The fall in blood pressure is due to a paralysis of the vasomotor center. Our findings do not agree with those of Domrich,[4] who permitted experiments to be made on himself and who found that with avertin alone the blood pressure decreased only slightly.

The venous blood pressure rose slightly in ten cases, fell in three and remained unchanged in two. In three of the cases in which there was a rise there was straining when the needle was inserted into the vein. In eight cases determinations were not made after four hours of anesthesia. The average venous pressure before anesthesia was 5.5 cm. of water, with a high value of 9 and a low value of 3. At the end of one hour of anesthesia the average venous pressure was 6.9 cm., with a high value of 12 and a low value of 3.5. At the end of four hours the average venous pressure was 5.3 cm., with a high value of 9 and a low value of 3. There were an average rise of venous pressure of 1.4 cm. within one hour and an average fall of 0.2 within four hours. Venous pressures were determined by the direct method, the venous puncture being made in the median basilic vein of the left arm at a level with the heart.

According to Eyster,[5] the venous pressure under basal conditions in normal persons is usually from 4 to 6 cm. The upper limit of normal is 11 cm.

Basal Metabolism.—Studies of basal metabolism are shown in table 4. In six of the cases determinations were not made after four hours of anesthesia. In all of the cases the basal metabolism dropped.

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2. Ransom, H. K.: Avertin as an Anesthetic for General Surgery, Arch. Surg. **26**:89 (Jan.) 1933.

3. Taylor, G. W., and Lund, C. C.: Blood Pressure Fall Occurring in Avertin Anesthesia, New England J. Med. **206**:612, 1932.

4. Domrich: Action of Avertin on Circulation, Zentralbl. f. Chir. **55**:2632, 1928.

5. Eyster, J. A. E.: Clinical Aspects of Venous Pressure, New York, The Macmillan Company, 1929.

TABLE 4.—*Basal Metabolism*

Case	Before Anesthesia	1 Hour of Anesthesia	4 Hours of Anesthesia
1	— 5	—15	—11
2	—12	—28	....
3	+17	—19	....
4	0	— 8	....
5	+ 5	— 8	....
6	—10	—25	—13
7	+10	—23	0
8	+ 3	—24	—19
9	+ 2	—14	—12
10	— 7	—38	—16
11	+ 7	— 5	— 5
12	+33	— 7	—10
13	+12	—21	+ 2
14	— 6	—26	....
15	+16	— 3	....
Averages	+ 4	—18	— 9

TABLE 5.—*Blood Chemistry*

Case	Time	Urea, Mg. per 100 Cc.	Sugar, Mg. per 100 Cc.	Carbon Dioxide, per Cent of Volume	Cholesterol, Mg. per 100 Cc.	Cholesterol Ester, Mg. per 100 Cc.	Ester Content, per Cent	Calcium, Mg. per 100 Cc.	Chlorides, Mg. per 100 Cc.
1	Before anesthesia	10	85	60.2	180	125	69	....	550
	1 hour of anesthesia	9	105	57.0	156	72	46	....	538
	4 hours of anesthesia	10	70	55.0	144	50	34	....	561
2	Before anesthesia	16	100	57.5	310	200	65	13.6	526
	1 hour of anesthesia	13	100	52.5	350	225	64	12.6	535
	4 hours of anesthesia	15	115	51.0	350	230	66	10.8	526
3	Before anesthesia	20	100	....	170	110	65	10.9	538
	1 hour of anesthesia	20	80	....	180	80	62	10.6	500
	4 hours of anesthesia	19	78	....	130	70	54	....	515
4	Before anesthesia	11	75	56.5	120	75	63	10.4	492
	1 hour of anesthesia	13	75	51.5	125	70	56	10.0	468
5	Before anesthesia	24	75	52.5	200	145	50	10.5	550
	1 hour of anesthesia	24	95	54.0	285	150	53	10.6	560
	4 hours of anesthesia	24	85	56.0	280	120	43	10.7	550
6	Before anesthesia	12	90	60.5	230	135	59	....	508
	1 hour of anesthesia	9	110	60.5	200	110	55	....	585
	4 hours of anesthesia	10	90	58.5	200	115	57	....	585
7	Before anesthesia	12	120	58.0	220	105	47	10.4	527
	1 hour of anesthesia	13	130	57.0	190	105	55	10.4	504
	4 hours of anesthesia	13	105	55.0	180	90	50	10.6	515
8	Before anesthesia	17	95	56.5	197	105	53	8.4	560
	1 hour of anesthesia	17	85	58.5	183	98	54	9.7	560
	4 hours of anesthesia	15	80	56.5	160	100	63	10.6	560
9	Before anesthesia	14	90	61.0	200	106	41	9.5	525
	1 hour of anesthesia	20	95	60.0	268	164	61	9.8	540
	4 hours of anesthesia	21	80	57.0	280	208	74	9.7	550
10	Before anesthesia	12	95	59.0	204	148	73	10.8	540
	1 hour of anesthesia	12	105	57.0	218	154	71	10.9	550
	4 hours of anesthesia	13	80	59.0	200	143	72	10.9	555
11	Before anesthesia	9	105	57.5	210	156	74	7.5	575
	1 hour of anesthesia	9	115	55.5	200	148	74	10.5	565
	4 hours of anesthesia	10	100	53.5	206	150	73	10.4	585
12	Before anesthesia	11	105	58.0	198	140	71	10.2	570
	1 hour of anesthesia	11	105	57.0	204	136	67	9.8	560
	4 hours or anesthesia	12	120	55.5	190	136	72	9.9	550
13	Before anesthesia	13	95	50.0	145	104	72	9.7	585
	1 hour of anesthesia	13	95	47.5	136	89	65	9.7	555
	4 hours of anesthesia	13	70	47.5	144	61	42	8.8	535
14	Before anesthesia	17	115	54.5	335	225	67	11.1	570
	1 hour of anesthesia	15	120	52 0	280	190	68	10.9	560
	4 hours of anesthesia	10	110	55.0	310	200	65	10.3	525
15	Before anesthesia	18	95	52.0	210	160	76	10.4	550
	1 hour of anesthesia	16	100	50.0	210	145	69	10.4	570
	4 hours of anesthesia	17	80	49.0	195	130	67	10.2	540
Averages									
	Before anesthesia	14	96	56.7	219	136	63	10.3	550
	1 hour of anesthesia	14	101	55.0	209	129	61	10.5	547
	4 hours of anesthesia	14	90	54.5	212	129	59	10.3	548

The average basal metabolism before anesthesia was +4 per cent, with a high value of + 33 and a low value of — 12. At the end of one hour the average basal metabolism was — 18, with a high value of — 3 and a low value of — 38. At the end of four hours the average basal metabolism was — 9, with a high value of + 2 and a low value of — 19. The average fall in basal metabolism was 22 per cent in one hour and 13 per cent in four hours. The most marked fall in basal metabolism was in case 12, in which there was a fall of 40 per cent. The patient had a basal metabolism of + 33 before anesthesia.

The studies in basal metabolism were carried out with the Benedict-Roth apparatus. A characteristic basal metabolic graph is presented.

Blood Chemistry.—The blood chemistry is shown in table 5. The figures for urea were remarkably constant, there being no variations in the averages for the preliminary observation, nor for the observations made at the end of one and four hours. The individual variations were slight and were always within the margin of experimental error, and the resultant gives a flat figure of 14 mg. per hundred cubic centimeters of blood for all three periods.

Waters and Muehlberger[6] and Stander[7] found no significant changes in the figures for blood nitrogen, but the complicating factor of operation was present in Waters and Muehlberger's seven cases and that of supplementary narcotics in Stander's five cases.

The blood sugar showed a slight initial rise and a slight terminal fall, being 5 mm. per hundred cubic centimeters higher at the end of one hour than at the outset and 6 mm. lower at the end of four hours. The highest individual rise was 20 mm. after one hour of anesthesia, and the greatest fall, 25 mm. after four hours.

Under the conditions described in the papers of Waters and Muehlberger and Stander a rise in blood sugar was found. We can say that the rise in blood sugar is purely an effect of the avertin.

The carbon dioxide content of the blood showed a slight tendency to fall, the average figures being 56.7 volumes per cent at the preliminary determination, 55 volumes per cent after one hour of anesthesia and 54.5 volumes per cent after four hours. The total fall was 2.2 volumes per cent. This is a slight change. The greatest fall was 6.5 volumes per cent. In two cases the carbon dioxide content rose slightly. The lowest recorded figure is 47.5 volumes per cent.

According to Wymer and Fuss,[8] who studied four cases of avertin anesthesia, there were the following changes in the acid-base balance: The

6. Waters, R. M., and Muehlberger, C. W.: Tribromethanol Anesthesia, Arch. Surg. **21**:887 (Dec.) 1930.

7. Stander, H. J.: Studies in Avertin, Am. J. Obst. & Gynec. **22**:219, 1931.

8. Wymer, I., and Fuss, H.: Acid Base Balance and Pathologic Physiology in Avertin Narcoses, Deutsche Ztschr. f. Chir. **211**:281, 1928.

alkali reserve (the carbon dioxide-combining power of the plasma) fell to below normal after the anesthesia; after varying periods of time it returned to, but did not exceed, the normal. There was never an increase of the alkali reserve above normal.

The reaction of the urine was shifted in the acid direction, the acidification lasting from twenty-four to forty-eight hours. The ammonia content of the urine was increased after the anesthesia; it fell, but did not reach normal within twenty-four hours. Wymer and Fuss concluded that the fall in alkali reserve with increased acidity of the urine and increased ammonia content was caused by true acidosis. Practically, the danger of acidosis is not great if the regulatory mechanism, particularly the kidneys and the respiratory center, are normal. In seven cases Achelis [9] found a lowering of the alkali reserve of from 2 to 6.6 volumes per cent.

The blood cholesterol averages were 219 mg. per hundred cubic centimeters for the preliminary reading, 209 mg. for the determination made after one hour, and 212 mg. for that made after four hours. The cholesterol esters were 136, 129 and 129 mg., respectively, for the same periods, representing an ester percentage of the total cholesterol of 63, 61 and 59 per cent, respectively. These figures were fairly constant.

We were particularly interested in these findings because of recent work showing the importance of the cholesterol and the cholesterol ester content of the blood plasma in determining hepatic damage (Thannhauser and Schaber [10] and Epstein [11]). The liver is the main excretory organ of cholesterol and regulates the relative content of cholesterol and cholesterol ester in the blood; 1 molecule of cholesterol is compounded with 1 molecule of fatty acid. In 100 cc. of normal human blood plasma there is from 150 to 200 mg. of total cholesterol, of which from 50 to 70 per cent is in the form of cholesterol ester. The aforementioned authors showed that in cases of hepatic damage the values for cholesterol ester were below those for free cholesterol, and that in the more severe cases the esters were much diminished or absent. The disappearance of the cholesterol ester occurs when the liver loses its ability to esterify the free cholesterol.

The figures for blood calcium showed little variation, the average figures being 10.3, 10.5 and 10.3 mg. per hundred cubic centimeters, respectively, for the preliminary determination and for the determinations made after one hour and after four hours.

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9. Achelis: Acid Base Relations and Operative Risk, Narkose u. Anaesth. **11**:541, 1928.

10. Thannhauser, S. J., and Schaber, H.: Studies in Blood Cholesterol, Klin. Wchnschr. **5**:252, 1926.

11. Epstein, E. Z.: Cholesterol of the Blood Plasma in Hepatic and Biliary Diseases, Arch. Int. Med. **50**:203 (Aug.) 1932.

The chlorides in the blood were similarly constant, the average figures being 550, 547 and 548 mg. per hundred cubic centimeters, respectively, for the preliminary observation and for the determinations made after one hour and after four hours.

In summing up the changes in blood chemistry, we should say that the urea, cholesterol and cholesterol ester, calcium and chlorides did not change appreciably, and that a minimal early rise and subsequent fall in the sugar content and a slight fall in the carbon dioxide content took place.

Plasma Volume.—The plasma volume as determined by the hematocrit in twelve of fifteen instances showed a rise, which in the extreme instance reached 9 per cent (table 6). In only two instances was there a fall. The average rise from the preliminary determina-

TABLE 6.—*Percentage of Plasma Volume*

Case	Before Anesthesia	1 Hour of Anesthesia	4 Hours of Anesthesia
1	55	58	60
2	60	54	55
3	55	60	60
4	55	64	63
5	60	66	63
6	57	60	57
7	53	60	62
8	60	63	61
9	56	58	59
10	55	54	55
11	63	63	68
12	58	61	63
13	64	66	67
14	63	64	65
15	64	66	66
Averages	59	61	62

tion to that made after four hours was 3 per cent. In most instances the dilution was greater after four hours than after one hour, although this finding was not constant. The average figures are 59, 61 and 62 per cent, respectively, for the preliminary determination and for the determinations made after one hour and after four hours.

Hematologic Studies (table 7).—In this group five cases were studied. The determinations were made before anesthesia was given and again two hours after the administration of the avertin. There were no significant changes in the hemoglobin and in the number of red cells.

In three cases there was a rise in the platelet count, and in two a fall. The average platelet count was 266,000 before anesthesia, as compared with 287,000 after two hours of anesthesia. The difference is slight.

In one case there was leukocytosis, the white blood count rising from 8,000 to 14,200. In all other cases there were only minor changes.

TABLE 7.—*Hematologic Studies*

Case		Before Anesthesia		2 Hours of Anesthesia	
7	Hemoglobin	102	per cent	104	per cent
	Red blood cells	5,300,000		5,500,000	
	Platelets	310,000		260,000	
	White blood cells	8,800		14,200	
	Differential:				
	Staff cells	5	per cent	5	per cent
	Segmented cells	69	per cent	74	per cent
	Eosinophils	0.5	per cent	1	per cent
	Basophils	1	per cent	0	per cent
	Lymphocytes	19.5	per cent	17	per cent
	Mononuclears	5	per cent	3	per cent
	Reticular cells	0.5	per cent	0.5	per cent
	Coagulation time	10	minutes	4	minutes
9	Hemoglobin	92	per cent	93	per cent
	Red blood cells	5,170,000		5,200,000	
	Platelets	220,000		245,000	
	White blood cells	8,200		6,350	
	Differential:				
	Staff cells	11	per cent	4	per cent
	Segmented cells	50	per cent	60	per cent
	Eosinophils	5	per cent	8	per cent
	Basophils	1	per cent	0	per cent
	Lymphocytes	23	per cent	22	per cent
	Mononuclears	10	per cent	6	per cent
	Reticular cells	21	per cent	21	per cent
	Coagulation time	7	minutes	5	minutes
10	Hemoglobin	89	per cent	87	per cent
	Red blood cells	5,250,000		4,900,000	
	Platelets	250,000		250,000	
	White blood cells	6,400		4,600	
	Differential:				
	Staff cells	2	per cent	2	per cent
	Segmented cells	53	per cent	48	per cent
	Eosinophils	..		6	per cent
	Basophils	..		1	per cent
	Lymphocytes	41	per cent	38	per cent
	Mononuclears	4	per cent	5	per cent
	Reticular cells	0.5	per cent	0.5	per cent
	Coagulation time	7	minutes	4	minutes
11	Hemoglobin	85	per cent	84	per cent
	Red blood cells	4,500,000		4,250,000	
	Platelets	200,000		200,000	
	White blood cells	7,800		8,000	
	Differential:				
	Staff cells	4	per cent	8	per cent
	Segmented cells	66	per cent	67	per cent
	Eosinophils	..		1	per cent
	Basophils	..		..	
	Lymphocytes	22	per cent	22	per cent
	Mononuclears	8	per cent	2	per cent
	Reticular cells	0.5	per cent	1	per cent
	Coagulation time	4	minutes	4	minutes
13	Hemoglobin	83	per cent	85	per cent
	Red blood cells	4,390,000		4,620,000	
	Platelets	350,000		420,000	
	White blood cells	7,600		7,200	
	Differential:				
	Staff cells	..		4	per cent
	Segmented cells	65	per cent	68	per cent
	Eosinophils	3	per cent	1	per cent
	Basophils	..		1	per cent
	Lymphocytes	27	per cent	22	per cent
	Mononuclears	5	per cent	4	per cent
	Reticular cells	0.5	per cent	0.5	per cent
	Coagulation time	4.5	minutes	1	minute

Finaly [12] studied the white blood cells before and during avertin narcosis and found an increase in the total number of leukocytes. The average white cell count before the narcosis was 10,750, and during the narcosis, 16,600.

TABLE 8.—*Urinalysis*

Case	Time	Amount, Cc.	Specific Gravity	Reaction	Albumin	Sugar	Acetone	Diacetic Acid	Urobilin, Mg.	Microscopic
1	Before anesthesia....	180	1.014	Acid	0	0	0	0	0	Negative
	4 hours of anesthesia	200	1.010	Acid	0	0	0	0	0	Negative
2	Before anesthesia....	150	1.010	Acid	0	0	0	0	0	Negative
	4 hours of anesthesia	80	1.034	Acid	Trace	0	0	0	Faint trace	Few white blood cells
3	Before anesthesia....	75	1.032	Acid	Very faint trace	0	0	0	0	Negative
	4 hours of anesthesia	315	1.022	Neutral	Very faint trace	0	0	0	Faint trace	Negative
4	Before anesthesia....	175	1.020	Acid	0	0	0	0	0	Negative
	4 hours of anesthesia	75	1.044	Acid	0	0	0	0	0	Negative
5	Before anesthesia....	200	1.022	Alkaline	0	0	0	0	0	Negative
	4 hours of anesthesia	120	1.042	Acid	0	0	0	0	4.3	Moderate number of white blood cells
6	Before anesthesia....	110	1.020	Neutral	0	0	0	0	0	Negative
	4 hours of anesthesia	100	1.045	Neutral	0	0	0	0	Faint trace	Negative
7	Before anesthesia....	115	1.020	Acid	0	0	0	0	Faint trace	Negative
	4 hours of anesthesia	15	1.048	Acid	Faint trace	0	0	0	Faint trace	Few hyaline casts
8	Before anesthesia....	80	1.030	Acid	0	0	0	0	Faint trace	Negative
	4 hours of anesthesia	75	1.042	Acid	0	0	0	0	0	Negative
9	Before anesthesia....	100	1.022	Acid	0	0	0	0	Faint trace	Negative
	4 hours of anesthesia	75	1.040	Acid	0	0	0	0	Faint trace	Negative
10	Before anesthesia....	400	1.012	Acid	0	0	0	0	0	Negative
	4 hours of anesthesia	75	1.028	Acid	Very faint trace	0	0	0	0	Negative
11	Before anesthesia....	320	1.006	Acid	0	0	0	0	0	Negative
	4 hours of anesthesia	120	1.022	Acid	Very faint trace	0	0	0	0	Negative
12	Before anesthesia....	50	1.028	Acid	0	0	0	0	0	Negative
	4 hours of anesthesia	100	1.045	Acid	0	0	0	0	0	Negative
13	Before anesthesia....	300	1.006	Neutral	0	0	0	0	Trace	Negative
	4 hours of anesthesia	180	1.028	Acid	0	0	0	0	Trace	
14	Before anesthesia....	120	1.018	Acid	Very faint trace	0	Trace	Very faint trace	Faint trace	Negative
	4 hours of anesthesia	120	1.018	Acid	Trace	0	Trace	Very faint trace	Faint trace	Negative
15	Before anesthesia....	150	1.020	Neutral	Very faint trace	0	0	0	0	Negative
	4 hours of anesthesia	90	1.022	Neutral	Very faint trace	0	0	0	0	Negative

The variations in the differential blood counts were neither constant nor marked. The tendency was toward a slight increase in the leukocytic elements and a slight decrease in the monocytic elements. In one

12. Finaly, R.: Effect of Avertin on Liver Function, Beitr. z. klin. Chir. **149**: 329, 1930.

case there was eosinophilia of 6 per cent in a patient who had had no eosinophilia before the anesthesia was given.

The reduction in the clotting time is of interest. This was a constant finding. The average clotting time before anesthesia was six and one-half minutes; two hours after anesthesia it was three and one-half minutes. We do not know the reason for this lowering of the clotting time. Changes in the platelet count or in the blood calcium content do not explain the finding in these cases.

Finaly carried out studies of the coagulation time in thirty-eight cases. He found that it was decreased in twenty-seven cases, increased in five and unchanged in six. The average coagulation time before the narcosis was 10.2 minutes, and after the narcosis, 7.5 minutes. The decrease in the coagulation time was noted by another observer (La Cava [13]).

Urine.—The results of studies of the urine are shown in table 8. Examinations were made of specimens obtained before anesthesia and four hours after anesthesia. The average amount of urine secreted after four hours was 118 cc. The amount of urine before anesthesia, as given in table 8, was determined approximately four hours after the last voiding. There was an average decrease of about 50 cc. in the amount of urine after four hours of the avertin anesthesia.

Coincident with the relative oliguria, there was an increase in the specific gravity, the average before anesthesia being 1.018 and that four hours after anesthesia was started, 1.032. In four cases from a faint trace to a trace of albumin was found after four hours; this was not present before anesthesia. Sugar was absent in all of the cases. In one case acetone and diacetic acid were present, but they were present also before the anesthesia. In one case a few hyaline casts were found after four hours, and in two cases some white blood cells. In all of the cases the reaction of the urine after avertin was acid or neutral. In one case there was an appreciable amount of urobilin (4.3 mg.) in the urine after avertin anesthesia.

In his study of thirty-eight cases of avertin anesthesia, Finaly found acetone and diacetic acid in three cases which did not show them before the anesthesia. In all of the cases the specific gravity of the urine was increased. Urobilinuria was occasionally observed.

SUMMARY

In this study of fifteen cases of avertin anesthesia in normal persons, uncomplicated by operation, auxiliary medication or supplementary anesthesia, the effects of avertin were:

1. An average increase in the pulse rate of 16 per minute and an average increase in the respiratory rate of 6 per minute.

13. La Cava, G.: Clinico-Experimental Contribution to Basal Avertin Narcosis, Policlinico (sez prat.) **39**:210 (Feb. 8) 1932.

2. A decrease in the amplitude of respiration.

3. An average decrease of 1.3 F. in the rectal temperature.

4. An average decrease in the systolic blood pressure of 24 mm.

5. An average decrease in the basal metabolism of 22 per cent.

6. An average decrease in the clotting time of three minutes.

7. A slight early rise in the blood sugar, a slight fall in the carbon dioxide content of the blood and a slight rise in the plasma volume.

8. A negligible change or no change in the venous pressure, blood cholesterol and cholesterol ester, blood calcium, blood chlorides and formed blood elements.

9. Slight oliguria and an increase in the specific gravity of the urine.

10. Loss of the conjunctival and tendon reflexes, with a late preservation of cutaneous and pharyngeal reflexes.

11. Slight cyanosis in two instances, increase in the secretion of mucus in the pharynx in five instances and slight vomiting in three instances.

No untoward effects followed the use of avertin in the dosage employed in basal anesthesia.

GUNSHOT WOUNDS OF THE HEAD

AN ANALYSIS OF ONE HUNDRED AND FIVE CASES

JOHN V. GOODE, M.D.
DALLAS, TEXAS

This series of 105 cases of gunshot wounds of the head was collected from the records of the Cincinnati General Hospital from 1922 to 1932. The total mortality rate (80.2 per cent) for 96 craniocerebral injuries of this series is considerably higher than that found for the same type of injury sustained during the World War. Cushing,[1] reporting a series of 219 cases in which operation was performed in a casualty clearing station, found a total mortality rate of 32.4 per cent, or, excluding 22 scalp wounds, 35.5 per cent for all craniocerebral injuries. Jefferson,[2] reporting from a base hospital, found no deaths in 91 cases of injury to the head without dural penetration and a mortality rate of only 37.6 per cent in 79 cases with dural penetration. Both considered only operative cases; however, every patient not moribund is said to have been subjected to operation. Horrax,[3] also reporting from a base hospital, operated on 93 of 132 patients with craniocerebral injuries, with a mortality rate of 37.6 per cent. He stated that 31 of the 132 injuries were cranial fractures without injury to the dura, which in part explains the low total mortality rate of 36.3 per cent for the entire series. This figure, 36.6 per cent, is comparable to the total mortality rate of 80.2 per cent for the 96 craniocerebral injuries reported in this paper. There is no such great difference in results, however, when the operative mortality rate for this series—45.1 per cent—is compared to the operative mortality rates mentioned earlier. As all patients reported in this series were alive on admission, and as every patient whose condition offered any possible chance of recovery was operated on, this series is comparable to that reported by Cushing. Since the operative mortality rate of all four series is essentially the same, the doubled total mortality rate of this series must be accounted for by the fact that the wounds were more severe or, more likely, that patients were seen earlier; many in this

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From the Department of Surgery of the College of Medicine of the University of Cincinnati and the Cincinnati General Hospital.

1. Cushing, Harvey: A Study of a Series of Wounds Involving the Brain and Its Enveloping Structures, Brit. J. Surg. **5**:558 (April) 1918.

2. Jefferson: Brit. J. Surg. **7**:262, 1919 .

3. Horrax, G.: Observations on a Series of Gunshot Wounds of the Head, Brit. J. Surg. **7**:10 (July) 1919.

series would never have lived to reach the casualty clearing stations of the war. Cushing stated that few were operated on within the first twelve hours after injury, and many after an interval of twenty-four hours. In this series there were only 8 admitted later than one hour after injury.

Many cases showed no improvement regardless of the supportive measures that were employed. Of the 77 patients who died, 42.8 per cent died within two hours of admission and 90.9 per cent within twenty-four hours. These two factors, the early admission and the early death of so many patients in this series, probably explain best the high total mortality rate.

MATERIAL

Every case of gunshot wound of the head brought to the receiving ward of the Cincinnati General Hospital is seen promptly by a member of the surgical house staff. If the patient is alive he is sent directly to the wards. Those who were dead on arrival or who died in the receiving ward are not reported in this series. All histories except 8 stated that the interval between injury and admission was one hour or less. An analysis of the material for this series is best made by consulting the following:

	Cases	Per Cent
Sex		
Male	94	89.5
Female	11	10.5
Race		
White	86	81.9
Colored	19	18.1
Cause of injury		
Suicide	56	53.3
Manslaughter	32	30.5
Accident	13	12.4
Details unknown	4	3.8

It is interesting to note that of the 56 persons who attempted suicide only two were female and none was colored. Often the type of firearm used is not mentioned, but by far the majority of the wounds were caused by pistol bullets fired at close range. In general, pistols of low caliber, such as .22 and .32, were used except when the police using the .38 caliber service pistol were involved.

ANALYSIS OF GROUPS

1. *Gunshot Wounds of the Head with the Dura Intact.*—There were 13 instances of this type of injury. Nine involved only the scalp or face and required only débridement of the wound with primary suture. There were no deaths from these superficial wounds. Four of the 13 showed a fracture of the skull. One of the 4 died on the second day from cardiac decompensation. This patient had attempted suicide because of heart failure. The bullet opened both frontal sinuses and

exposed the dura, but did not injure it. Under local anesthesia the edges of the skin and bone were excised, small folded rubber protective drains were placed in the frontal sinuses, and the skin was closed loosely with fine black silk sutures. The dura was not opened.

2. Gunshot Wounds of the Head with Laceration of the Dura, But No Foreign Bodies in the Brain.—There were 9 instances of this type of injury, with 8 operations and no deaths. The 1 patient not operated on was shot through the base of the nose, the bullet entering on the left side, crossing the right side of the face and ending just beneath the skin below and behind the right ear. At first no craniocerebral injury was suspected, but on the second day blood-tinged cerebrospinal fluid drained from the left nostril. The drainage of spinal fluid continued for three or four days and then stopped spontaneously. This case was complicated by the development of an arteriovenous aneurysm in the right side of the neck beneath the bullet. The bullet was removed, fortunately without opening the arteriovenous communication.

In every case prompt operation was performed, with thorough débridement of skin, bone and cortex and suture of the dura and skin without drainage. In 1 instance, the dural defect was so great that a piece of fascia lata was used to effect a closure.

3. Gunshot Wounds of the Head with Subcortical Lodgment of Foreign Bodies.—This is the largest group of the series. There were 49 cases with 42 deaths, a total mortality rate of 85.7 per cent. Only 15 of the 49 patients were operated on, with an operative mortality rate of 60 per cent. A study of the type of wounds in this group reveals several interesting facts. There were only 5 with tangential or gutter-like wounds, with detached fragments of bone driven into the brain. Of these 5, 4 recovered. The remaining 44 patients had a bullet or bullets retained within the skull. As might be expected from the few instances of the gutter type of wound and the high percentage of cases of suicide, most of the wounds were found in the temporal region at the level of the ear, usually just in front of it. Three patients recovered without removal of the penetrating bullet; 2 of these received débridement of the wound of entrance with no attempt to remove the bullet, and 1 received no operative treatment.

This group of cases, with a mortality rate of 85.7 per cent, offers a difficult problem. That many are hopeless from the start is shown by the fact that only about one third of the total number came to operation. Preoperative roentgenograms should be made in every case in order that the number and position of foreign bodies may be determined. It is well to have blood typing done for transfusion if possible. The operation itself consists of careful débridement of skin, muscle and bone. The removal of the whole fractured portion of the skull *en bloc* has

not been carried out in this series. It is not so important to excise the edges of the torn dura, although this tissue may have to be incised further to control bleeding from the cortex and to allow thorough exploration and cleansing of the track of the bullet in the cortex. The cortical wound is best handled by the technic described by Cushing.[4] A catheter attached to a sterile syringe is used alternately to irrigate and to suck the devitalized brain tissue from the track of the bullet.

Most surgeons explore the wound once with the gloved index finger to be sure that no foreign bodies have been overlooked. In this series, whenever the dura could not be closed with fine black silk, a strip was taken from the fascia lata and sutured to the edges of the dural defect. The wounds were closed without drainage in all the patients who recovered, closure consisting of interrupted sutures of medium black silk in the galea and interrupted sutures of fine black silk in the skin. A light cast for the head is helpful, because often the patient is restless and may derange the dressings or injure the unprotected brain.

4. *Through-and-Through Gunshot Wounds of the Head.*—There were 34 cases in this group with a mortality rate of 100 per cent. Only four were operated on, and these lived for an average of four hours after operation. Other reports on through-and-through wounds of the head give an average mortality rate of about 80 per cent, but this rate is based on only those cases in which the ventricles were not penetrated. Cushing found a 100 per cent mortality rate in cases showing penetration of one or both ventricles by fragments of bullets. In this series probably most through-and-through wounds were associated with the penetration of the ventricular system, because many of the patients attempted suicide and consequently were shot at close range through the midportion of the brain. Only 3 came to autopsy, but all of these showed perforation of one or both lateral ventricles.

Immediate Complications.—Infection is the most dreaded complication of gunshot wounds of the head. There were 3 patients with complicating infections in this series. They were not admitted for treatment immediately after sustaining the injury, 1 coming to the hospital four weeks after an incomplete débridement elsewhere, 1 coming for treatment thirty-six hours after injury and 1 being admitted sixteen hours after injury. There was no instance in the entire series of infection with Clostridium Welchii, although this complication was noted frequently in reports dealing with cranial injuries sustained during the World War. Meningitis developed in 2 patients.

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4. Cushing, Harvey: Notes on Penetrating Wounds of the Brain, Brit. M. J. 1:221 (Feb. 23) 1918.

REPORTS OF CASES

CASE 1.—J. S., a Negro, aged 25, was admitted to the Cincinnati General Hospital four weeks after having been shot by a .38 caliber pistol. The wound of entrance was in the right temporal region 2 inches (5 cm.) above the right ear; the wound of exit was 2 inches above the left eye. Superficial débridement with a suture of the skin was carried out in another hospital. The patient stated that he remained unconscious for four days and was discharged after two weeks. For the next two weeks he had a mild frontal headache. For ten days prior to admission, there had been a clear watery discharge from both nostrils.

On admission the patient was fully conscious, but somewhat confused. There were no visual disturbances and no weakness. The temperature was 99 F., and the pulse rate, 80. During his stay in the hospital only a slight amount of clear nasal discharge was noticed. Eight days before death, the patient became comatose and had a slight fever, but showed no localizing signs. Two days before death definite signs of meningitis developed; the spinal fluid showed gram-positive cocci and 2,000 polymorphonuclear leukocytes. A needle was inserted through one of the bullet wounds, but no abscess was located.

Autopsy revealed the right frontal sinus filled with pus communicating through several cracks with a large abscess in the right frontal lobe. There were also signs of early lobular pneumonia.

CASE 2.—L. E., a Negress, aged 13, was admitted to the Cincinnati General Hospital thirty-six hours after being shot with a .22 caliber pistol. The wound of entrance was just above and medial to the right eye. There was no wound of exit. The temperature was 100.2 F.; the pulse rate 128 and the respiratory rate, 22. The patient was comatose and showed unmistakable signs of meningitis. There was a continuous drainage of clear spinal fluid from the right nostril. Cisternal drainage was carried out, but the patient died the next day. Autopsy showed that the right cribriform plate had been perforated by the bullet, which was lodged in the brain just behind the optic chiasm. Early meningitis apparently took its origin from an abscess that surrounded the bullet.

CASE 3.—One patient who recovered was admitted to the hospital sixteen hours after receiving a gutter-like wound in the forehead. Débridement of the wound was performed under local anesthesia; the devitalized brain tissue was washed away, the bone fragments were removed, the dura was sutured as well as possible and the skin closed with fine black silk. An extradural infection developed which required treatment with surgical solution of chlorinated soda. The patient was discharged on the twenty-first day with a granulating wound of the forehead.

CASE 4.—One patient who had attempted suicide received a penetrating wound of the left side of the forehead. Thorough débridement, with removal of the fragments of bone and the devitalized brain tissue and transplantation of the fascia without drainage, was the surgical procedure. The bullet, shown by roentgenograms to be under the left temporal lobe, was not removed. On discharge five weeks after injury the patient showed no localizing signs, but there was definite mental instability. This mental instability has persisted for eleven years. It is not enough, however, to prevent the patient from doing housework. It manifests itself in crying spells, poor memory and a feeling that she is going to lose her mind. There is apparently no desire to repeat the attempt at suicide.

CASE 5.—In another case a fistula developed in the occipital region from which cerebrospinal fluid drained. The fistula developed eight days after operation and drained for two weeks without causing serious complications. The bullet was

flattened against the skull, the dura being punctured in one place by a sharply depressed fragment of bone. The puncture was closed with fine black silk sutures. There was no infection present at any time.

Follow-Up Results.—Because this series extends over eleven years and because many of the patients who survived were transients, the follow-up results are very disappointing. Only 4 patients could be found for reexamination. All 4 were classified in group 3, showing gunshot wounds of the head, with subcortical lodgment of foreign bodies. Two of the 4 still have bullets lodged in the brain (1 after ten years and 1 after eighteen months), but in neither of these are there any symptoms referable to the retained bullet. Two show hemiplegia, but this condition seems to be improving with exercise. There is no instance of headache, fainting or epileptic seizures. One patient who left the hospital with pronounced diplopia and sensory aphasia was completely relieved of symptoms in six months.

COMMENT

This study emphasizes the importance of considering the interval of time between injury and admission for treatment before drawing any comparisons as to total mortality rates in reports on gunshot wounds of the head. This is particularly true in comparing reports on injuries in the war, few of which were seen in the first twelve hours, with reports of gunshot injuries of the head encountered in civil life, of which the vast majority are seen in the hospitals within the first hour. The fact that of the 77 deaths reported here 90.9 per cent occurred in the first twenty-four hours shows how the amazing total mortality rate of 80.2 per cent can be found in a large municipal hospital, in which most injuries by gunshot are seen immediately after injury.

The high percentage of suicide, 53.3, is startling. If the figures are analyzed by years no marked increase is noted in the past four years. However, the largest number for any one year was found in 1932, in which there were 8 cases marked suicide, 4 marked accident and 2 marked manslaughter. It is likely that the high percentage of cases of suicide explains in part the relatively infrequent occurrence of the gutter type of gunshot wounds of the head (5) and also the high percentage of cases with retained bullets in the brain. Since the former is the most favorable and the latter the least favorable condition the total mortality rate of 85.7 per cent for gunshot wounds of the head with subcortical lodgment of foreign bodies is at least partially explained.

This study of cases reveals again the well known danger of infection in patients who are not operated on early. There was no instance of infection by Cl. Welchii probably because the operations were performed within the first few hours. There were 3 patients with cerebrospinal

rhinorrhea, 2 of whom died of meningitis; the other underwent no operation for the gunshot wound but recovered completely. In spite of the 1 recovery, cerebrospinal rhinorrhea should be considered as of grave prognostic significance.

Many authors believe that retained foreign bodies lead to traumatic epilepsy; some believe that foreign bodies should always be removed—if not at the primary operation, certainly at some later date. The follow-up data in this report are too meager to justify the expression of an opinion on this question, but 2 patients reporting for reexamination showed how difficult the decision of this question may be. One had had a bullet in the cranial cavity for over ten years, and the other for over one year, but neither showed any symptoms referable to the bullet. Both were told the first symptoms of intracranial pressure and were instructed to report to the hospital should any of the symptoms develop. Perhaps this is begging the question, but it is difficult to decide to perform a craniotomy to search for a bullet that is causing no demonstrable trouble.

SUMMARY

1. A study of 105 cases of gunshot wounds of the head is reported. Of these, there were 96 cases of craniocerebral injury.

2. The total mortality rate for the cases of craniocerebral injury was 80.2 per cent; for the 31 cases in which an operation was performed, it was 45.1 per cent.

3. All except 8 patients were admitted to the hospital within one hour after the injury. Of the 77 deaths, 42.8 per cent occurred within two hours and 90.9 per cent within twenty-four hours.

4. The high death rate in this series as compared with the statistics of the World War is undoubtedly due to the immediate hospitalization of all patients.

5. In this series of 105 cases, there were 56 attempts at suicide—53.3 per cent.

6. As recorded in all other studies, infection was the main cause of death among patients who did not die as a direct result of the injury.

QUANTITATIVE STUDY OF THE RATE OF HEALING IN BONE

I. DESCRIPTION OF METHOD

WILLIAM T. PEYTON, M.D.

ULYSSES S. ANDERSON, M.D.

AND

CARL W. LAYMON, M.D.

MINNEAPOLIS

Some time ago (1929) it was decided to check the results of some experiments in which it had been reported that the rate of healing in bone could be influenced by certain variations in the experiment. Although careful studies have been carried out by different investigators to determine the influence of a certain substance or condition on the healing of bone, the conclusions drawn by these investigators are variable and in some instances in direct conflict. It appears probable that the cause of these conflicting results is due in large part, if not entirely, to the difficulty of estimating the amount of healing which has taken place at any given time after fracture has occurred or has been produced for experimental purposes. Clinically, it is impossible to be certain when a fracture is healed sufficiently to allow resumption of function. For this reason certain minimum limits of time have been set more or less arbitrarily for each type of fracture. These limits are based on the experience that angulation or displacement may occur if function is resumed earlier. The appearance of the repair as seen in roentgenograms is of value in observing the amount of repair and in estimating its strength, but since the method is based entirely on opinion, it is inaccurate. Several roentgenologists reading the same roentgenogram would give very different estimates of the strength of a given callus. Delayed union is also an unreliable measure of the healing of bone. There are various degrees of delayed union and a difference of opinion exists even as to when union is delayed. Nonunion is, of course, a definite entity when it does occur, but like delayed union it would serve only as a gross indicator when used to interpret experimental results.

In most experimental investigations the healing of bone has been based on the evidence of callus formation as seen in the roentgenogram. This gives no evidence of the early fibrous callus before calcium salts are deposited in it and an inaccurate estimate of the strength of the healing fracture later when calcium salts are being deposited.

From the Department of Surgery, University of Minnesota.

METHOD

A method was therefore evolved to measure the strength of the callus throughout the healing process, as well as to determine when the healing process is complete. Since the first union is fibrous, it offers little or no resistance to a shearing force, but it does have tensile strength. Later, when calcium salts are laid down in the callus there is an appreciable resistance to shearing forces. The method evolved was therefore designed to measure tensile strength, resistance to bending and resistance to torsion.

To measure tensile strength it was necessary to devise a method of suspending the bone by one end and hanging weights on the other until the bone was broken. Resistance to bending and torsion in metal rods and beams is measured by the physicist and expressed as coefficients of bending and torsion. An attempt was made to determine the coefficients of bending and torsion for healing bone by the method and formula used for metal, but this was found impracticable because of the variable shapes of bones. It seemed that more reliable conclusions could be obtained by keeping the mechanical factors of the experiment as constant as possible and by treating the data obtained statistically. Certain modifications in the apparatus and method used by the physicist had to be worked out in order to adapt them to the process of measureing the ulna of the rabbit.

Since this study was begun quantitative studies concerning the resistance of healing bone to a shearing force have been reported by Lindsay and Howes [1] and by McKeown and others,[2] and a study of resistance to compression has been reported by Ross.[3]

Material.—Rabbits receiving the ordinary laboratory diet were used. No attempt was made to select animals of the same size, age, or weight. The ulna was used so that the radius would act as a natural splint, obviating the necessity of artificial splints for immobilization and permitting the animal to be about in normal fashion immediately after the bone was fractured.

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1. Lindsay, M. K., and Howes, E. L.: The Breaking Strength of Healing Fractures, J. Bone & Joint Surg. **13**:491, 1931.

2. McKeown, R. M.; Lindsay, M. K.; Harvey, S. C., and Howes, E. L.: The Breaking Strength of Healing Fractured Fibulae of Rats: II. Observations on a Standard Diet, Arch. Surg. **24**:458 (March) 1932. McKeown, R. M., Lindsay, M. K.; Harvey, S. C., and Lumsden, R. W.: The Breaking Strength of Healing Fractured Fibulae of Rats: III. Observations on a High Fat Diet, ibid. **25**:467 (Sept.) 1932; The Breaking Strength of Healing Fractured Fibulae of Rats: IV. Observations on a High Carbohydrate Diet, ibid. **25**:722 (Oct.) 1932; The Breaking Strength of Healing Fractured Fibulae of Rats: V. Observations on a Low Calcium Diet, ibid. **25**:1011 (Dec.) 1932.

3. Ross, Dudley: A Method for the Production of Increased Compression Strength of Bones, Brit. J. Surg. **22**:337, 1932.

Technic.—The technic of fracturing the bone was simple. The rabbits were anesthetized with ether, the hair was removed from one of the forelegs by means of barium sulphide, the skin prepared with iodine and alcohol, and the leg protected by a sterile drape. A longitudinal incision, about 3 or 4 cm. long, was made on the lateral aspect, the fascia was divided, and the muscles were retracted. The middle of the ulna was exposed and cut through by means of a sterile circular bone saw. As a rule no hemostasis was required, since there was little bleeding. The fascia and the skin were closed with interrupted linen sutures. The animals experienced little reaction from the procedure and behaved quite normally after one or two days. They were allowed to survive a varying number of days before they

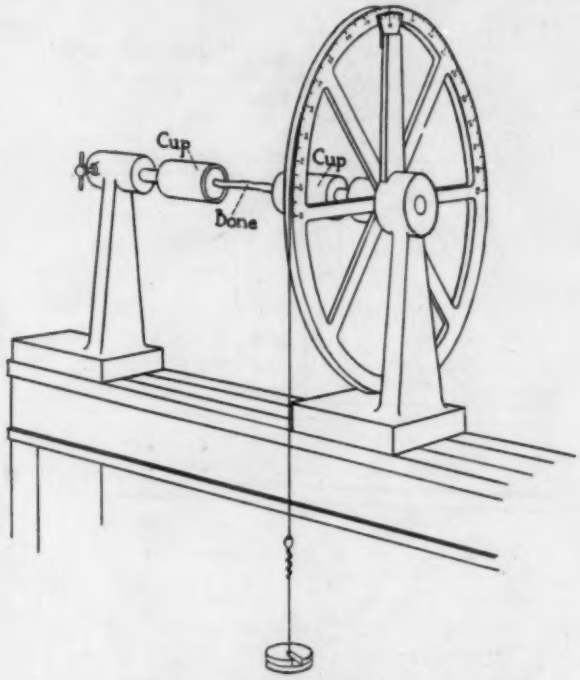

Fig. 1.—Method of measuring resistance to torsion.

were killed. Routine autopsy was not done, but rabbits in which evident intercurrent disease developed were discarded.

Measurements.—Both ulnas were removed, weighed and measured immediately after the animal was killed. As a rule the measurements were taken on the fractured and on the normal ulna of each rabbit. Occasionally, measurements could not be made on both ulnas for various reasons, such as an accident to one of the bones during the process of measuring, or infection of the fracture. The total length and the largest and smallest diameters at the middle of the bone were determined in centimeters by means of calipers. The average of the last two measurements was determined. A metal cup was then placed over each end of the bone and fixed firmly in place by means of plaster of paris. The cups were so constructed that they would fit in the apparatus for measuring torsion and could be

used in suspending the bone by one end and applying weight to the other in measuring breaking strength. After the bones had been placed in the cups, the length of the exposed bone, i. e., the distance between the inner edges of the cups, was measured. This distance was kept as constant as possible and, although recorded for most of the experiments, it was not utilized in the analysis of data.

Torsion.—In measuring torsion, the same apparatus as that used by the physicist to determine the coefficient of torsion in a metal rod was used (fig. 1). The cups were fitted into this apparatus while the plaster of paris was still soft, and they were left until it had set. Then weights were applied and readings were taken.

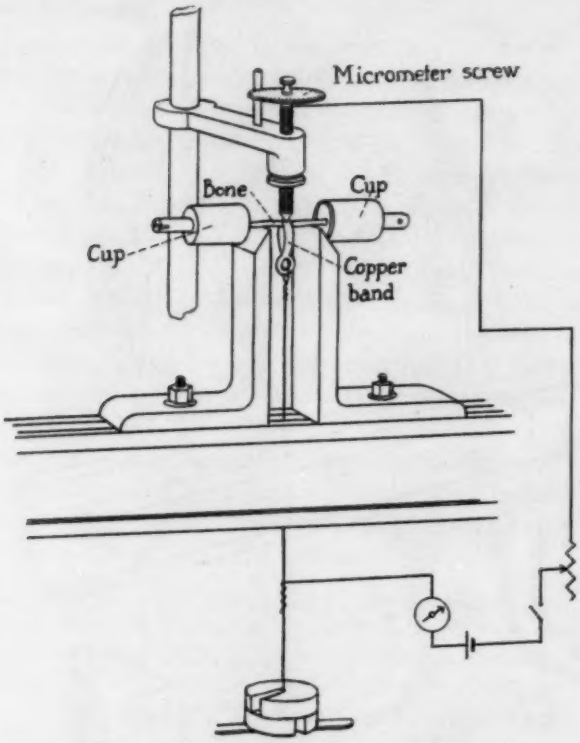

Fig. 2.—Method of measuring resistance to bending.

Readings were again taken as the weights were removed. For this part of the experiment it was important that the bones were firmly fixed in the cup, in order that no rotation could occur, and at the same time it was essential that the material used to fix the bone was removable. Plaster of paris seemed to fulfil these requirements better than any other material.

Bending.—The apparatus for measuring bending strength (fig. 2) consisted essentially of two parallel metal supports on which the bone rested and of a micrometer screw placed over the bone, which could be screwed down into contact with the bone, both before and after bending by the addition of a known weight. The weight was attached to a copper band hung over the bone at the midpoint between the rests. The number of revolutions or the part of a revolution of the

micrometer screw required to bring it against the bone determined the amount of bending. Turning the micrometer scale 1 degree moves its point approximately 0.005 mm. In order to be certain that the point of the micrometer screw was in contact with the bone the end-point was determined by establishing an electrical contact. This was accomplished by using electric current from a battery, one terminal of which was connected through a resistance to the micrometer screw and the other through a galvanometer to the copper band on which the weight was suspended. The supports were beveled so that the bone rested on very small

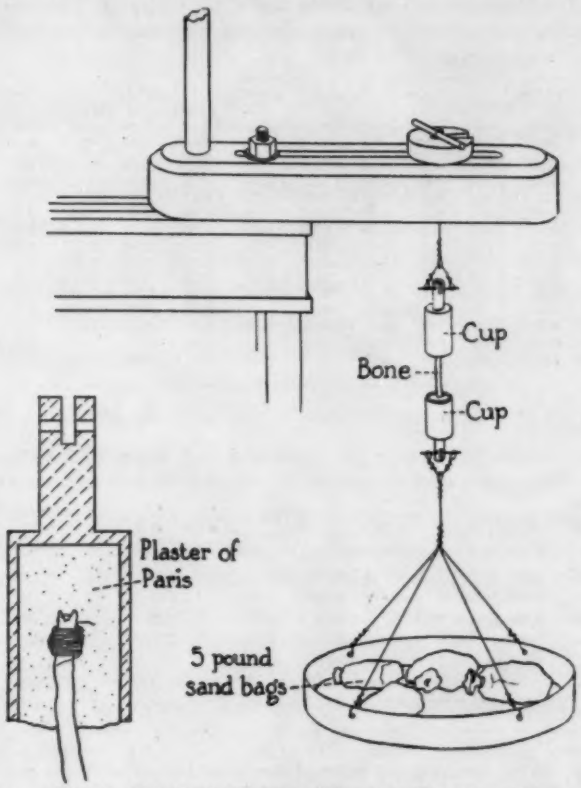

Fig. 3.—Method of determining tensile strength.

surfaces. The distance between these supports was kept constant. The bones were all placed in relatively the same position on the supports. The amount of bending was obtained both on adding and on removing weights.

Tensile Strength.—Tensile strength was ascertained in a rather simple manner (fig. 3). The metal cups were left in place and one of these was attached to a beam extending over the edge of the table, while a pan on which weights could be placed was attached to the other cup. Sacks of sand of 5 pounds (2.268 Kg.) each were added to the pan until the bone was broken. In some of the experiments the distal end of the ulna pulled out of the plaster, but it was found that this could be prevented by winding soft wire tightly around this end of the bone before it was embedded in the plaster of paris.

RESULTS

Measurements were recorded on the right and left ulnas of thirteen rabbits taken without selection from the stock supply of animals. In this experiment only one reading each for bending and torsion was recorded. These readings were taken after adding 500 Gm. of weight The results of the experiments are recorded in table 1.

TABLE 1.—*Measurements on Right and Left Ulnas of Thirteen Rabbits*

Right Ulna							Left Ulna						
Greatest Diameter	Least Diameter	Width of Cortex	Weight of Bone	Torsion	Bending	Breaking	Greatest Diameter	Least Diameter	Width of Cortex	Weight of Bone	Torsion	Bending	Breaking
0.55	0.22	0.05	2.082	0.4	0.50	92.0	0.56	0.22	0.04	2.020	0.4	0.30	89.00
0.49	0.23	0.04	1.167	0.5	1.50	79.5	0.50	0.23	0.06	1.210	0.5	2.0	89.75
0.48	0.20	....	1.006	1.0	3.75	59.5	0.50	0.21	0.07	1.556	1.4	3.75	69.50
0.45	0.22	0.08	1.124	0.6	6.00	34.0	0.46	0.21	0.06	1.092	1.2	2.0	39.00
0.52	0.28	....	1.282	0.6	2.00	30.0	0.49	0.30	....	1.220	0.7	5.0	35.00
0.54	0.25	0.04	1.637	0.6	0.50	55.0	0.56	0.27	0.06	1.707	0.6	1.5	34.00
0.54	0.28	0.04	1.517	0.6	4.50	59.5	0.55	0.27	0.04	1.545	0.5	2.5	64.50
0.50	0.24	0.09	1.462	0.5	2.00	97.5	0.49	0.26	0.08	1.532	0.4	2.5	97.50
0.48	0.26	0.06	1.425	0.4	1.25	69.0	0.49	0.28	0.08	1.422	0.3	1.5	97.50
0.47	0.23	0.05	1.110	0.9	3.50	48.0	0.48	0.24	0.07	1.286	0.9	7.5	94.00
0.50	0.26	0.06	1.691	0.7	4.50	54.0	0.50	0.27	0.05	.....	0.3	1.5	15.00
0.58	0.30	0.05	1.676	0.9	3.00	60.0	0.58	0.31	0.05	1.721	0.9	6.0	60.00
0.44	0.23	....	1.134	1.1	4.00	54.0	0.44	0.25	0.05	1.105	1.0	3.5	54.00

TABLE 2.—*Statistical Constants for Right and Left Ulnas of Thirteen Rabbits* *

Dimension	Right Ulna Mean ± PE_m	Left Ulna Mean ± PE_m	Difference $M_r - M_l$	$PE_{mr}^2 + PE_{ml}^2$ (PE)	Difference / PE	Right σ	Left σ
Greatest diameter	0.503 ± 0.0075	0.510 ± 0.0062	−0.007	0.0097	−0.721	0.0386	0.0322
Least diameter...	0.246 ± 0.0056	0.256 ± 0.0064	−0.010	0.0085	−1.176	0.0290	0.0326
Width of cortex..	0.056 ± 0.0039	0.063 ± 0.0026	−0.007	0.0047	−1.489	0.0171	0.0127
Weight of bone...	1.457 ± 0.0571	1.451 ± 0.0575	+0.006	0.0800	+0.075	0.2930	0.2826
Torsion.....	0.680 ± 0.0450	0.700 ± 0.0680	−0.020	0.0820	−0.244	0.2291	0.3488
Bending.....	2.850 ± 0.3280	3.040 ± 0.4000	−0.190	0.5170	−0.368	1.0825	2.0550
Breaking.....	60.920 ± 5.5350	64.520 ± 5.4320	−3.600	7.7550	−0.464	28.4231	27.9024

* M_r represents the mean of measurements on the right leg; M_l, the mean of measurements on the left leg; PE_{mr}, the probable error of the mean for measurements on the right leg; PE_{ml}, the probable error of the mean for measurements on the left leg; σ, the standard deviation.

The statistical constants for these data (table 2) show that there is no significant difference between the right and the left ulna. This signifies that it is legitimate to use one leg as a control for experiments on the other.

Measurements have also been taken of a series of bones in which the right ulna was fractured and the left ulna used as a control. These results will be given in a later report.

HEPATOLIENOGRAPHY

EXPERIMENTAL STUDY OF THE ELIMINATION OF THE CONTRAST MEDIUM

H. HAMILTON COOKE, M.D.
LOWVILLE, N. Y.

The development of an accurate, harmless method for the visualization of the liver and spleen has been for many years a challenge to the radiologist, internist and surgeon. Information about the size, shape, position, relation and structure of these organs would be of great value in the investigation and interpretation of almost all diseases of the abdominal viscera. If, in addition, it were possible to detect such pathologic conditions as neoplasms, abscesses, malformation, injuries and decreased, increased or abnormal function of these organs, many lives could be saved and much suffering alleviated by earlier and more exact treatment. It is, however, reasonable and necessary to insist that no matter how excellent the diagnostic method, it must not endanger the health or life of the patient.

Progress in the roentgen visualization of the liver and spleen has been made by the intravenous injection of iron preparations, the intravenous injection of dyes excreted by the liver and the intraperitoneal injection of air. Recently Oka [1] and Radt [2] described a new method of hepatolienography by the intravenous injection of a colloidal solution of thorium dioxide. Several hundred papers have appeared in the literature dealing with various phases of this method. A considerable difference of opinion exists as to the radioactivity, distribution and immediate and late toxic effects of this material. It seems to me that the most important point to consider in accepting or rejecting this method is to determine whether the thorium is eliminated, and, if eliminated, by what organs and at what rate. If the material is toxic, a reliable means must be devised for its rapid and complete elimination. The present work is based on a review of all the available literature on the use of thorium dioxide in hepatolienography and on a group of experiments by which it was believed possible to investigate the rate of elimination of thorium dioxide from the body.

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1. Oka, M.: Eine neue Methode zur roentgenologischen Darstellung der Milz (Lienographie), Fortschr. a. d. Geb. d. Röntgenstrahlen **40**:497, 1929.

2. Radt, Paul: Eine Methode zur roentgenologischen Kontrastdarstellung von Milz und Leber, Klin. Wchnschr. **8**:2128, 1929.

REVIEW OF THE LITERATURE

While it has repeatedly been considered that thorium is eliminated by the lungs through cells contained in the bronchial mucus, by the liver through the bile, by the intestines through the feces and by the kidneys through the urine, nevertheless no definite proof or quantitative studies have been reported of actual adequate elimination by any organ. Oka,[1] in his original study of hepatolienography, by means of colloidal thorium dioxide noted severe hemoglobinuria in rabbits. The urine from these animals contained small amounts of thorium. It is possible that the thorium in the urine was derived directly from the blood plasma. In a later article, Oka [3] does not suggest the presence of any method of elimination of thorium either in animals or in man. Radt,[2] in his first descriptions of hepatolienography by the use of thorium, did not consider the problem of elimination. In a late contribution he [4] summarized his experiences of three and a half years of experimental hepatolienography with thorium dioxide in animals and two years of clinical work with seventy patients. No definite diminution in the intensity of the roentgen shadow of the liver and spleen could be detected in experimental animals eighteen months after the injection of the thorium. Patients observed over a long period showed no decrease in the density of the roentgen shadow of the liver or spleen. He concluded that both roentgen examination and histologic studies indicate a slow process of elimination by an unknown method. Dickson [5] believed that in rabbits the shadow of the liver is reduced 50 per cent in intensity during the first three months after the injection. He suggested that cells containing the granules of thorium are eliminated by passing into the lungs, after which they are carried to the exterior in the bronchial mucus. The same method has also been considered by Radt [6] and Kadrnka.[7] No diminution in the quantity of thorium stored in the spleen, bone marrow, lymph nodes and ovaries occurred in three months.

3. Oka, M.: Klinische Anwendung der "Lienographie," einer neuen Methode zur roentgenologischen Darstellung von Milz und Leber, Fortschr. a. d. Geb. d. Röntgenstrahlen **41**:892, 1930.

4. Radt, Paul: Zur Kontrastdarstellung von Leber und Milz (Hepato-Lienographie), Therap. d. Gegenw. **75**:348, 1932.

5. Dickson, W. H.: Thorotrast: A New Medium for Radiologic Diagnosis, Canad. M. A. J. **27**:125, 1932.

6. Radt, Paul: Ueber die körnige Ablagerung kolloider Farbstoffe in den Leberparenchymzellen von Kaninchen nach intravitaler Injektion (nach Versuchen mit Tusche und Eisen), Ztschr. f. d. ges. exper. Med. **69**:721, 1930.

7. Kadrnka, Silvije: Hepatosplenographie: méthode radiologique d'exploration du parenchyme hépatique et splénique par introduction intraveineuse de "Thorotrast," substance colloidale à base de dioxyde de thorium, Schweiz. med. Wchnschr. **61**:425, 1931.

Bungeler [8] observed definite roentgen shadows of the liver and spleen in animals twenty-one months after the injection of thorium. He did not recommend the use of thorium in hepatolienography so long as no information is available as to how long the thorium is retained. Kadrnka [9] considered the elimination of thorium from both experimental animals and man as very slow. The roentgen shadows produced by the thorium persisted for many months. The lungs were considered a possible means of elimination, but the rôle of the liver and kidneys could not be determined. Stewart [10] did not observe any evidence of a decrease in the intensity of the roentgen shadow of the liver and spleen in a patient observed for eight months. Naegeli [11] made microscopic examinations of the liver and spleen eighteen months after the injection of thorium into experimental animals. No decrease in the quantity of thorium granules was observed. Popper [12] injected thorium intravenously into twelve patients, four of whom were examined at necropsy. In one patient who died two months after the injection, a chemical analysis showed 97 per cent of the thorium present in the liver and spleen, while 3 per cent was recovered from the bone marrow. Examination of patients who had received injections of thorium four months previously and of animals which had received injections seven months previously showed no diminution in the roentgen shadow of the liver or spleen. Leipert [13] made a chemical analysis of the thorium contents of various organs of experimental animals and of man. He found that patients who received injections two, four and sixty days previous to necropsy showed 64.3, 56.9 and 97 per cent of thorium in the spleen, liver and bile. Rabbits receiving injections twenty-eight, sixty-seven and ninety-eight days previous to examination showed 48.5, 98.9 and 70.8 per cent of thorium in the liver, spleen and lungs. He concluded that detached reticulo-endothelial cells containing thorium are eventually lodged and retained in the spleen. The possibility of elimination through the liver by means of the bile

8. Bungeler, W., and Krautwig, J.: Ist die Hepato-Lienographie mit Thorotrast eine unschädliche diagnostische Methode? Klin. Wchnschr. **11**:142, 1932.

9. Kadrnka, Silvije: Hepatosplenography, Roentgenologic Demonstration of the Parenchyma of the Spleen and Liver by Means of a New Intravenous Contrast Medium (Thorotrast), Radiology **18**:371, 1932.

10. Stewart, W. H.; Einhorn, Max, and Illick, H. E.: Hepatography and Lienography Following the Injection of Thorium Dioxide Sol (Thorotrast), Am. J. Roentgenol. **27**:53, 1932.

11. Naegeli, Lauche: Ueber experimentelle und pathologisch-anatomische Untersuchungen bei Kontrastdarstellung der Milz und Leber, Med. Klin. **28**:1878, 1931.

12. Popper, H. L., and Klein, Erwin: Ueber Hepato-Lienographie, München. med. Wchnschr. **78**:1829, 1931.

13. Leipert, Theodor: Ueber die Verteilung des Thorium im Organismus nach Injektion von Thorotrast, Wien. klin. Wchnschr. **44**:1135, 1931.

was considered greater than through the kidneys. Einhorn [14] injected thorium dioxide into seven patients. No definite evidence of elimination could be detected by roentgen studies of the liver and spleen. Whitaker [15] observed no diminution in the shadow of the liver in a patient six months after the injection of thorium dioxide. It appears from the literature that roentgen studies, microscopic observations and chemical examinations of organs, bile, sputum, feces and urine furnish no evidence of a physiologic mechanism for the adequate elimination of thorium dioxide from the body.

METHOD AND RESULTS OF EXPERIMENT

Twenty rabbits were used in this investigation. The animals varied from 1,625 to 3,200 Gm. in weight. In each animal 2.5 cc. of colloidal thorium dioxide per kilogram of body weight was injected intravenously. All the injections were made with aseptic technic in the veins of the ear, but in some animals it became necessary to use the veins in the extremities. Roentgen examinations were made of the living animals at irregular intervals, and of the organs at necropsy. All the roentgenograms were made by a standard technic. The animals were kept on the usual diet.

Roentgen Observations.—Group I: Preliminary studies were made on ten rabbits. Roentgenograms were made on the first, seventh, fifteenth, thirtieth, and forty-fifth days after the last intravenous injection of the thorium dioxide. All roentgenograms taken twenty-four hours after the last intravenous injection of 2.5 cc. of colloidal thorium dioxide per kilogram of body weight showed the liver and spleen as smooth, clearcut shadows of homogeneous density. The position, size, shape and margins of the organs were accurately outlined. In some animals the spleen showed small punctate areas of increased density, especially near the periphery. In the roentgen shadows of the liver it was possible, in a few animals, to see a fan-shaped area which apparently represented the course of the larger vessels. Roentgenograms taken fifteen, thirty and forty-five days after the injection showed no evidence of definite diminution in the density of the hepatic and splenic shadow. In the small animals it was also possible to observe definite shadows produced by the kidneys, suprarenal glands and marrow of the larger bones. When more than 10 cc. of colloidal thorium dioxide per kilogram of body weight was injected distinct roentgen shadows were produced by the lungs, suprarenal glands, kidneys and marrow of the larger bones.

Group II: In rabbits 7 (male, weighing 1,800 Gm.) and 2 (male, weighing 1,860 Gm.) roentgenograms of the liver and spleen were made twenty-four hours after the intravenous injection of thorium dioxide. One daily intravenous injection of 100 cc. of 0.9 per cent saline solution was given for fourteen consecutive days. Roentgen examinations were then made on the following day, and fifteen and

14. Einhorn, Max; Stewart, W. H., and Illick, H. E.: Experiences with Uroselectan Sodium, Skiodan and Thorotrast, M. J. & Rec. **134**:56, 1931.

15. Whitaker, P. H.; Davis, T. B., and Murgatroyd, F.: Hepato-Lienography by the Aid of Thorotrast; Its Uses and Dangers, Quart. J. Med. **5**:34, 1933.

thirty days later. The roentgenograms taken on the first, fifteenth and thirtieth days after the injection of 100 cc. of 0.9 per cent saline solution showed no evidence of any diminution in the size, shape and density of the shadow obtained twenty-four hours after the injection of thorium dioxide.

Fig. 1 (rabbit 36).—Hepatolienography forty-five days after a total intravenous injection of 10 cc. of a colloidal solution of thorium dioxide per kilogram of body weight.

Fig. 2 (rabbit 36).—Roentgenogram of the liver, spleen, lungs, kidneys, suprarenal glands and right posterior extremity forty-five days after the injection of thorium dioxide.

Fig. 3 (rabbit 31).—Hepatolienography forty-five days after the intravenous injection of 2.5 cc. of thorium dioxide per kilogram of body weight.

Group III: In rabbits 9 (female, weighing 2,025 Gm.) and 13 (female, weighing 2,250 Gm.) roentgen examination of the liver and spleen was made twenty-four hours after the injection of thorium dioxide. The animals were given one daily intravenous injection of 100 cc. of 10 per cent solution of dextrose for fourteen consecutive days. Roentgen examinations were then made on the first, fifteenth and thirtieth days. The roentgenograms taken after the injection

of 100 cc. of 10 per cent solution of dextrose for fourteen consecutive days showed no apparent diminution in the density of the shadow produced by the liver and spleen twenty-four hours after the injection of thorium dioxide.

Group IV: In rabbits 1 (male, weighing 2,540 Gm.) and 12 (female, weighing 2,530 Gm.) roentgenograms of the liver and spleen were made twenty-four hours after the intravenous injection of thorium dioxide. One daily intravenous injection of 100 cc. of a 5 per cent solution of calcium chloride in 0.9 per cent saline solution was given for fourteen consecutive days. Roentgen examination was made on the following day and fifteen and thirty days later. There was no evidence of any diminution in the intensity of the roentgen shadow of the liver and spleen following the intravenous injection of solution of calcium chloride for fourteen consecutive days.

Fig. 4. (rabbit 7).—Hepatolienography forty-five days after the intravenous injection of 2.5 cc. of thorium dioxide per kilogram of body weight and fourteen daily intravenous injections of 0.9 per cent saline solution.

Fig. 5 (rabbit 7).—Roentgenogram of the organs removed at necropsy, forty-five days after the intravenous injection of thorium dioxide and thirty days after the intravenous injection of saline solution.

Group V: In rabbits 14 (male, weighing 2,700 Gm.) and 3 (female, weighing 2,740 Gm.) roentgenograms of the liver and spleen were made on the day following the intravenous injection of thorium dioxide. One daily subcutaneous injection of 0.2 cc. of combined typhoid vaccine was given for fourteen consecutive days. Roentgen examination was made on the following day and fifteen and thirty days later. Following the subcutaneous injection of 0.2 cc. of typhoid vaccine for fourteen consecutive days roentgen examination of the liver and spleen showed no evidence of any diminution in the size, shape and density of the shadow obtained twenty-four hours after the intravenous injection of thorium dioxide.

Group VI: In rabbits 16 (female, weighing 2,540 Gm.) and 17 (female, weighing 2,250 Gm.) roentgenograms of the liver and spleen were made twenty-four

hours after the injection of thorium dioxide. The animals received one daily subcutaneous injection of 0.25 cc. of epinephrine for fourteen consecutive days. Roentgen examination was made on the following day and fifteen and thirty days later. There was no definite evidence of any diminution in the roentgen shadow of the liver and spleen following the subcutaneous injection of 0.25 cc. of epinephrine as compared with the density of the shadow obtained twenty-four hours after the injection of thorium dioxide.

Microscopic Study.—Sections of the liver, spleen, suprarenal glands and kidneys were made from the animals in group I, one, fifteen, thirty and forty-five days after the injection of thorium dioxide. All the sections were stained with hematoxylin and eosin. The granules of thorium were observed in the reticulo-endo-

Fig. 6 (rabbit 12).—Hepatolienography forty-five days after the intravenous injection of 2.5 cc. of thorium dioxide per kilogram of body weight and thirty days after fourteen daily intravenous injections of a 5 per cent solution of calcium chloride in 0.9 per cent saline solution.

Fig. 7 (rabbit 12).—Roentgenogram of the liver, spleen, lungs, kidneys, suprarenal glands and right tibia forty-five days after the intravenous injection of a solution of calcium chloride.

thelial cells of the spleen, liver, suprarenal glands and lungs, while in the kidneys the granules of thorium were located in the cells of the glomerular tuft. The thorium was not stained and appeared as higly refractive small granules. There was no evidence of any diminution in the quantity of the granules of thorium in the phagocytic cells of the liver, spleen, suprarenal glands or kidneys forty-five days after the intravenous injection. Microscopic examination of the liver, spleen, suprarenal glands, lungs and kidneys from the animals in groups II, III, IV, V and VI forty-five days after the intravenous injection of the thorium dioxide showed no distinct evidence of any diminution in the amount of granules of thorium in the liver, spleen, lungs, suprarenal glands or kidneys as compared with the amount of granules of thorium found in the same organs of the animals in group I.

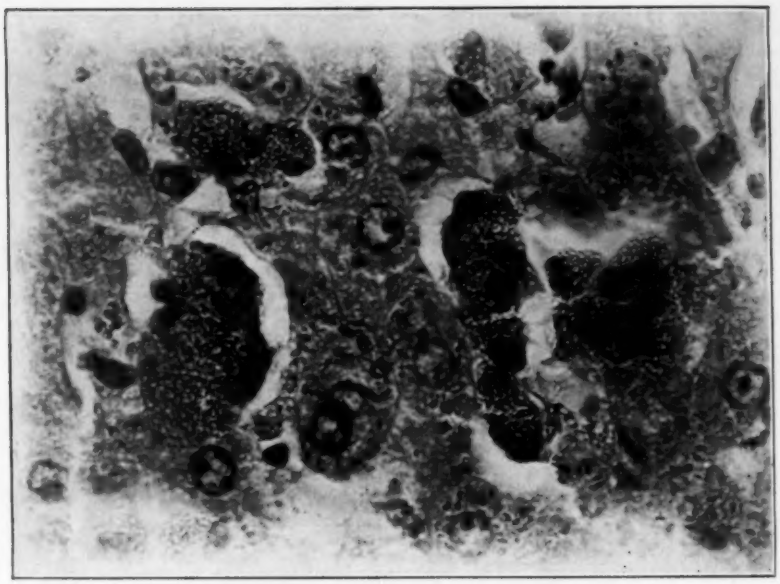

Fig. 8.—Granules of thorium in the Kupffer and hepatic cells; × 800.

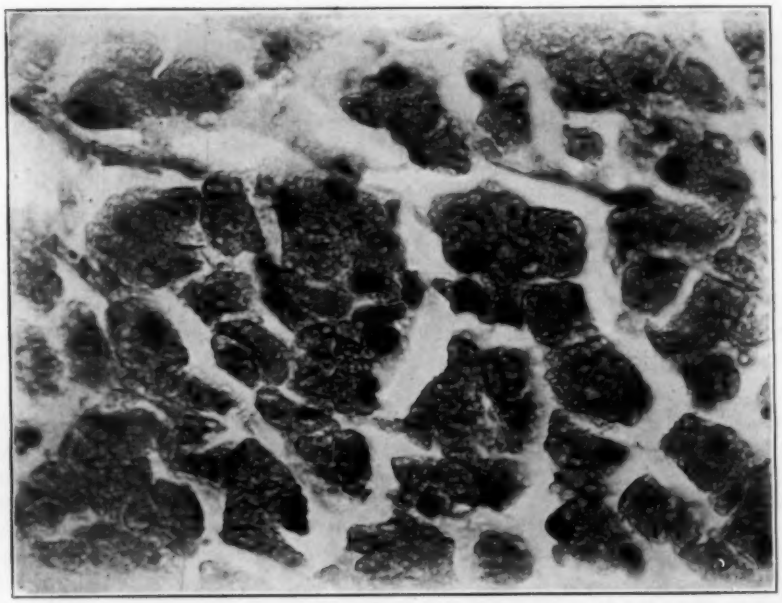

Fig. 9.—Granules of thorium in the reticulo-endothelial cells of the spleen; × 800.

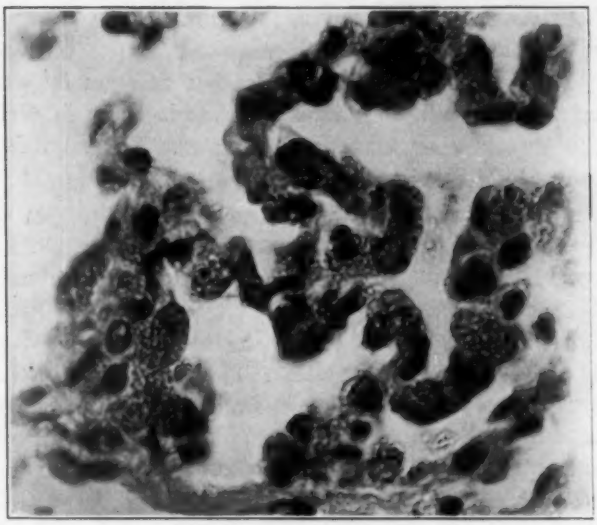

Fig. 10.—Granules of thorium in the phagocytic cells of the lungs; × 800.

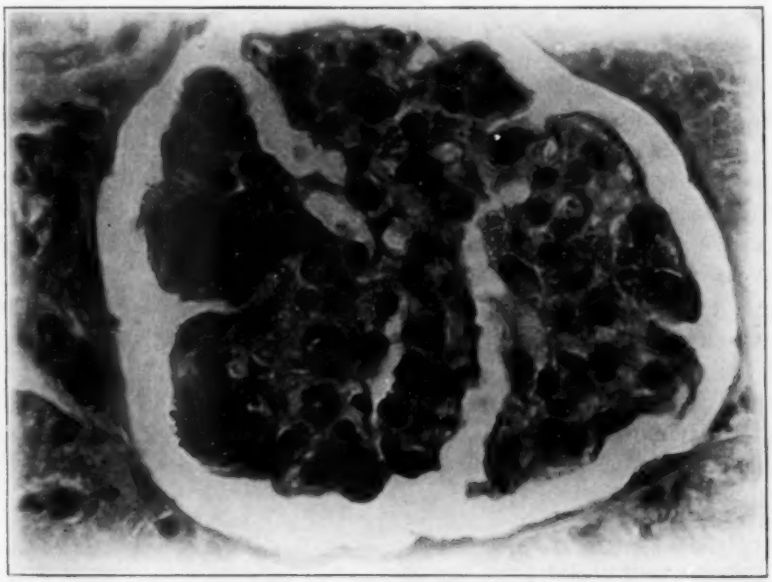

Fig. 11.—Granules of thorium in the phagocytic cells of the glomerular tuft; × 800.

COMMENT

The thorium preparation used in this work consisted of a stabilized solution of thorium dioxide which contained 25 per cent of thorium dioxide by volume and about 20 per cent of thorium by weight. The material mixed well with the blood and was injected in divided doses without any difficulty or immediate reaction. The animals appeared normal during the entire period of observation.

Following an intravenous injection granules of thorium are rapidly removed from circulation. No granules of thorium could be detected in the plasma five minutes after the first intravenous injection of 2.5 cc. of colloidal thorium dioxide per kilogram of body weight. The thorium is removed from the circulation by the anchored phagocytic cells of the reticulo-endothelial system. The importance of this efficient mechanism for removing particulate material from the circulating blood has been investigated by numerous workers. Goldman [16] was apparently the first to emphasize the importance of, and call attention to the widespread distribution of, a system of cells in various organs of the body which have essentially the same function. It remained, however, for Aschoff [17] to present the collected evidence that there exists in the body an anatomically extensive and functionally important group of highly differentiated cells which manifest such striking similarities in their reactions to vital stain and granular material as to warrant their consideration as a unit. An unusual peculiarity of the constituent cells of this system is their distribution in a number of organs such as the spleen, liver, bone marrow, medulla of the suprarenal gland and lungs instead of localization in a definite fixed circumscribed area. According to Aschoff the basis for the inclusion of a cell or cell group as a portion of the reticulo-endothelial system is the marked ability to phagocytose rapidly and to retain granular material. Aschoff used the term "reticulo-endothelial system" in a limited and in a broad sense. In the limited sense it is composed of two groups of cells: (1) the reticulum cells of the splenic pulp, the cortical nodules and pulp cords of the lymph nodes and the lymphoid apparatus; (2) the reticulo-endothelial cells of the sinuses of the capillaries of the bone marrow, the suprarenal cortex and the hypophysis. In a broad sense the constituent cells of the reticulo-endothelial system include the reticulum cells, the reticulo-endothelial cells, the tissue histiocytes and the phagocytic monocytes of the circulating blood.

16. Goldman, E.: Die äussere und innere Secretion des gesunden und kranken Organismus im Lichte der "vitalen Färbung," Beitr. z. klin. Chir. **64**:1, 1909.

17. Aschoff, Ludwig: Ueber die Lipoidinfiltration in den Kupfferschen Sternzellen und in den Retikulumzellen der Milz, und Beziehungen zu den Xanthelasmen, Ber. d. Naturw. gesellsch. z. Freiburg **20**:66, 1913.

While the physiology of the reticulo-endothelial system is not well understood, Aschoff,[18] Maximow,[19] Schittenhelm[20] and Jaffe evaluate the function of the reticulo-endothelial system as the most important factor in all general defensive reactions. It is the only mechanism by which particulate material such as bacteria, pigment and dead cells can be removed from the circulation. The phagocytic reticulo-endothelial cells located in the liver, spleen, bone marrow and lungs remove the greater portion of thorium from the blood stream. Smaller quantities are phagocytosed by the reticulo-endothelial cells of the suprarenal glands, ovaries and kidneys. The dispersion and deposition of the particles of thorium cannot be controlled after they reach the circulating blood. The location of the thorium depends on its direct contact with and phagocytosis by the reticulo-endothelial cells of the various organs. The liver, spleen and bone marrow possess the largest divisions of the reticulo-endothelial system and will, under normal conditions, phagocytose the largest number of particles of thorium. The density of the roentgen shadow is in direct proportion to the quantity of thorium in the cytoplasm of the reticulo-endothelial cells of the organ. The liver, spleen and bone marrow present, therefore, a denser shadow than the lungs, suprarenal glands, kidneys or ovaries. The roentgenograms of the liver, spleen, bone marrow, kidneys and suprarenal glands made forty-five days after the intravenous injection of thorium showed no difference in the density of the shadows when compared with similar films taken twenty-four hours, fifteen and thirty days after the injection of thorium dioxide. The microscopic examination of the liver, spleen, lungs, suprarenal glands and kidneys fifteen, thirty and forty-five days after the injection of thorium dioxide showed no evidence of a decrease in the quantity or redistribution of the thorium as compared with similar examinations twenty-four hours after the injection. It was believed possible by intravenous or subcutaneous injection of various substances to stimulate any existing process of elimination and to observe any redistribution of the particles of thorium present in the reticulo-endothelial cells of the various organs. However, even after the daily intravenous injection of 100 cc. of a 0.9 per cent saline solution for fourteen days it was not possible to detect any immediate or late roentgen evidence of any diminution in the quantity of thorium in the liver, spleen or other organs. The density of the roengenograms made forty-five days after the

18. Aschoff, Ludwig: Das reticulo-endotheliale System, Ergebn. d. inn. Med. u. Kinderh. **24**:1, 1924.

19. Maximow, Alexander: Macrophages or Histiocytes: Special Cytology, New York, Paul B. Hoeber, Inc., 1928, p. 426.

20. Schittenhelm, A.: Normale und pathologische Physiologie des reticulo-endothelialen Systems, in Handbuch der Krankheiten des Blutes und der Blutbildenden Organe, Berlin, Julius Springer, 1925, vol. 2, p. 492.

injection of thorium was identical with that of films made twenty-four hours after the injection. Similar observations were made after the use of a 10 per cent solution of dextrose, a 5 per cent solution of calcium chloride, typhoid vaccine or epinephrine. Not only the roentgenograms of the liver and spleen of the live animals, but those of the organs removed at necropsy produced shadows of identical density, regardless of the time which had elapsed. The microscopic studies showed an approximately similar quantity and location of the granules of thorium in the cytoplasm of the reticulo-endothelial cells of the various organs when compared with the observations in the control group (I). Since the intensity of the shadow of the liver and spleen produced by the thorium depends on the presence of the granules of thorium in the reticulo-endothelial cells of those organs, it is evident that if the reticulo-endothelial cells are not actively phagocytic or injured, the smaller amount of material would be phagocytosed and the roentgen shadow would be less intense. It appears from this investigation that the particles of thorium are permanent inclusions.

While the reticulo-endothelial system has important functions, the effects of the thorium have to be considered not only as the direct effect on the reticulo-endothelial cells, but also as possible indirect functional effects on the cells of the organs of which the reticulo-endothelial cells are only a part. Thus the effect of the thorium on the liver cannot be considered as limited to the Kupffer cells, since possible effects on the hepatic cells and their function must be weighed. This consideration becomes especially important when one observes the presence of particles of thorium in such important and sensitive structures as the suprarenal glands and ovaries. While thorium has not been considered radioactive by some investigators, doubt entertained in this regard by competent workers makes it necessary to realize fully that once thorium is phagocytosed by the reticulo-endothelial cells, it is apparently permanently fixed in the body. The thorium cannot be eliminated or redistributed by the means used in this experiment. The realization that the thorium remains fixed in the reticulo-endothelial cells should emphasize the careful selection of cases for the use of this material. The intravenous injection of large doses for diagnostic purposes ought to be limited to patients in whom, after every other diagnostic method has been exhausted, the additional information proves the necessity for immediate surgical treatment.

CONCLUSION

Marble-like roentgen shadows of the liver and spleen of rabbits can be obtained by the intravenous injection of 2.5 cc. of colloidal thorium dioxide per kilogram of body weight. The thorium is removed from the circulation by the phagocytic reticulo-endothelial cells located prin-

cipally in the liver, spleen and bone marrow. Some thorium is deposited in the lungs, suprarenal glands, kidneys and ovaries. Roentgen and histologic examination showed no evidence of elimination or redistribution of thorium in ten rabbits forty-five days after the injection. Fourteen daily injections of 100 cc. of a 0.9 per cent saline solution, a 10 per cent solution of dextrose, a 5 per cent solution of calcium chloride, 0.2 cc. of combined typhoid vaccine or 0.25 cc. of epinephrine did not eliminate or redistribute the thorium dioxide. Since the health and life of the patient may be jeopardized by the prolonged presence of particles of thorium in the vital organs, the intravenous injection of thorium dioxide for diagnostic purposes should be restricted until some positive method of rapid elimination has been discovered.

ACCESSORY ARTICULAR PROCESSES OF THE LUMBAR VERTEBRAE

W. S. FULTON, M.D.
AND
W. K. KALBFLEISCH, M.D.
WHEELING, W. VA.

In these days of traumatic injuries and subsequent legal entanglements it is of considerable importance for the surgeon and roentgenologist to know about possible anomalies of the skeletal system and to be able to distinguish them from supposed fractures. Improved roentgenographic technic allows one to visualize a given bone with much more detail than was possible in the not too distant past. Hence it is a natural tendency to diagnose a demonstrated separation of continuity in a bone as a fracture if the history of an accident makes such a diagnosis plausible. This applies especially to alleged fractures of processes of the vertebrae. For technical and anatomic reasons the articular processes of the vertebrae are difficult to demonstrate. It is here that misinterpretation may not infrequently be met with and discussions arise as to whether an abnormal condition is present and, if so, whether the abnormality represents a traumatic or a congenital lesion.

In 1933, Rendich and Westing [1] (to the best of our knowledge, for the first time in the American literature) called attention to an abnormality of the articular processes of the lumbar vertebrae, which they described as a "separate ossicle occurring at the lower end of the inferior articular processes of the second and third lumbar vertebra"; they added five cases of their own to the two cases previously reported in the German literature. Undoubtedly findings of this sort have been encountered in every roentgen laboratory, but they were probably always diagnosed as fractures, if circumstances warranted it.

It may be well to review the known facts concerning the diagnosis of accessory articular processes of the lumbar vertebrae. In 1931, at the twenty-second congress of the German Roentgen Society, Reisner,[2] presented a paper entitled "How to Distinguish Normal, Inflammatory

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From the Wheeling Clinic.

1. Rendich, R. A., and Westing, S. W.: Accessory Articular Process of the Lumbar Vertebrae and Its Differentiation from Fracture, Am. J. Roentgenol. **29**:156, 1933.

2. Reisner, A.: Unterscheidungsmerkmale normaler, entzündlicher und posttraumatischer Zustände an der Wirbelsäule, Fortschr. a. d. Geb. d. Röntgenstrahlen **44**:726 (Dec.) 1931.

and Post-Traumatic Conditions of the Spine." In the paper he mentioned a case in which a gap across the right lower articular process of the second lumbar vertebra was accidentally found. There was no history of trauma, and the patient did not complain of pain in the back. Because of the perfectly smooth outline of the edges of the bone and the absence of displacement of the distal fragment, and of atrophy, Reisner considered the case one of an accessory articular process. In his discussion of the case, Grashey stated that he had seen the same abnormality several times, and that he differentiated it emphatically from a fracture.

In the same journal appeared a paper by Müller,[3] describing a case of formation of a gap through the left lower articular processes of the second lumbar vertebra. Four weeks previous to the examination, the patient had fallen down a flight of stairs; the examination was undertaken to find a possible cause of the indefinite pains in the back. In this first publication Müller considered the finding to be an *Umbauzone,* the result of an injury with attempted repair through formation of connective tissue in the bone. One year later, in a second publication—after hearing Reisner's paper and Grashey's discussion, we venture to say—Müller[4] reconsidered the diagnosis and felt inclined to look at the case as an anomaly—an accessory articular process. In February, 1933, Rendich and Westing published the reports of five cases of formation of a gap through the lower articular processes of the lumbar vertebrae; they expressed the opinion that they were dealing with congenital lesions rather than fractures. In two of their cases no history of trauma was obtainable. Two patients received a possible injury to the back on the day of the examination, and another patient had received one four days before. All of the patients, however, complained of vague pains in the back with various localizations, and all had various degrees of limitation of motion. The roentgenograms of the spines of all of the five patients showed gaps through one or two articular processes, with well defined, smooth, regular edges of cortical density. Although an old ununited fracture may give a similar picture, three of Rendich and Westing's patients had sustained injuries only a few hours or days previous to the examination, and it seems impossible that such changes, if due to a fracture, could have taken place within such a short interval. Therefore the diagnosis of fracture as a cause for the gaps seems unreasonable. Since there is no recognized separate epiphysis for the development of the tip of the articular process,

3. Müller, Walther: Spaltbildungen an Gelenk- und Dornfortsätzen der Wirbelsäule auf der Basis von Umbauzonen, Fortschr. a. d. Geb. d. Röntgenstrahlen **44**:644, 1931.

4. Müller, Walther: Ueber eine bemerkenswerte Form von Wirbelsäulenmissbildung, München. med. Wchnschr. **79**:356 (Feb. 26) 1932.

Rendich and Westing could classify their findings only as accessory ossicles at the articular processes.

The aforementioned publication brought to mind a case we saw in October, 1932.

Case 1.—A man, aged 49, a railroad employee, who, in October, 1931, was hit in the back by a slowly moving car, was referred to us for roentgenograms of the lumbar vertebrae and pelvis. He did not tumble over and, except for a short passing pain at the site of the impact, had no unusual sensations. He paid no attention to the accident and went on working without further complaint. After three months he began to notice vague pains in the back, which continued. He sought medical advice, but the pain did not yield to various methods of treatment.

The roentgenologic findings on Oct. 10, 1932, were as follows: The right and left lower articular processes of the third lumbar vertebra showed a distinct gap about 1 mm. wide and slightly curved, which was seen more clearly on the right than on the left, where the spinous process was somewhat overlapping. The smaller lower fragments were about 8 mm. in length. The bony edges of the larger and smaller fragments at the gap were perfectly smooth and showed cortical density. The smaller fragments did not present atrophy of the bone, displacement or evidence of formation of callus or of a spur of bone. The axis of the spine was straight. The only other pathologic finding in the spine was that the first sacral vertebra showed nonunion of the posterior arch.

With the history of the previous accident, the diagnosis was ununited fractures of the lower articular processes of the third lumbar vertebra and spina bifida occulta.

On reading Rendich and Westing's paper, we were struck with the similarity in roentgenologic appearance between their cases and the one reported here; the fact that our patient mentioned that he had no immediate pains in the back and had worked for three months after the accident without complaints increased our doubts as to whether we had diagnosed the condition correctly. In summary, the following facts presented themselves: The patient had received an injury to the back. The spine was not immobilized after the injury. After one year a roentgenogram showed complete separation of continuity in the bone substance of two articular processes of the third lumbar vertebra. There was no indication of callus formation, nor was there formation of a bony spur. Because the spine was not immobilized and because the patient was working, it might be assumed that union of the fractures did not occur, and that we had to deal with a case of pseudo-arthrosis. The smoothed edges of the fragments suited this diagnosis. From these data alone it was therefore possible to assume that during the accident the patient had received fractures of the lower articular processes of the third lumbar vertebra. In 1923, Koch [5] published the report of a case with the same end-results, except that a diagnosis of

5. Koch, Konrad: Die isolierten Gelenkfortsatzbrüche der Lendenwirbelsäule, Deutsche Ztschr. f. Chir. **180**:339, 1923.

fracture was made immediately after the accident and there was a slight displacement of the fragment. The fracture did not heal, but the edges of the fragments of bone became smoothed out. The patient

Fig. 1.—Formation of gap through the lower articular processes of the third lumbar vertebra.

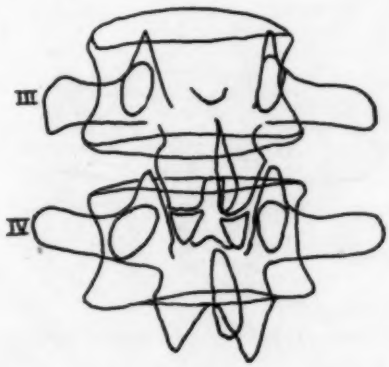

Fig. 2.—Diagram of the roentgenographic findings in case 1.

refused to be operated on and continued to complain of an indefinite "pain in the back."

On the other hand, there were features in our case which cast doubt on the diagnosis of fracture and made us lean toward the diagnosis of congenital malformation. It is reasonable to assume that an injury

severe enough to fracture two articular processes would give rise to immediate and pronounced symptoms, but they were absent and the man continued at his work. Koch reported that his patient was in a state of severe shock after the injury. One would also expect to find at least an irregularity, if not a displacement, of the small separated tips of the

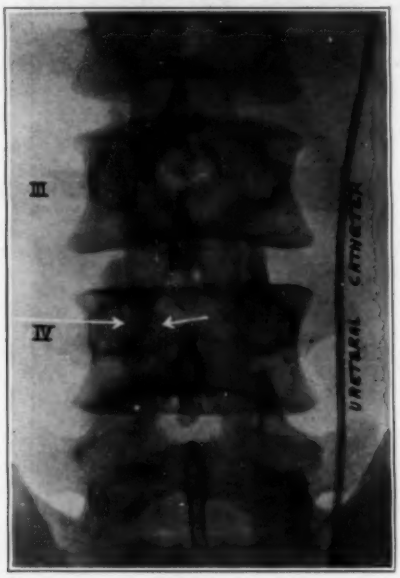

Fig. 3 (case 2).—Formation of a gap through the right lower articular process of the third lumbar vertebra.

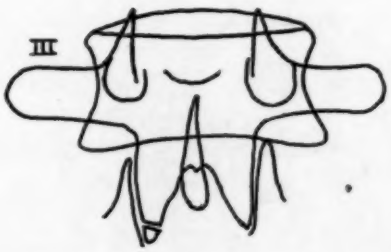

Fig. 4.—Diagram of the roentgenographic findings in case 2.

articular processes. Instead, their position was normal. Furthermore, the small, broken-off fragments might have shown atrophy after one year, but they were just as dense as the rest of the articular processes. In addition, the spine, as seen in both views, was straight. The finding of a spina bifida occulta in roentgenograms might give a hint as to the possibility of further developmental defects.

After a review of all of these facts and the arguments pro and con, it seemed that it might be impossible to convince the patient that he had only a congenital lesion of the third lumbar vertebra. In a legal case it might be just as impossible to demonstrate to a jury that there

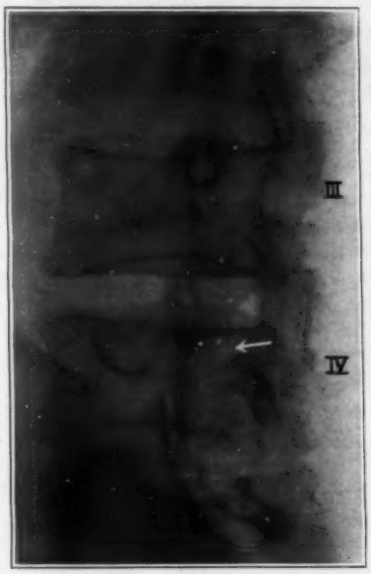

Fig. 5 (case 2).—Oblique view, with the patient rotated 45 degrees on the right side.

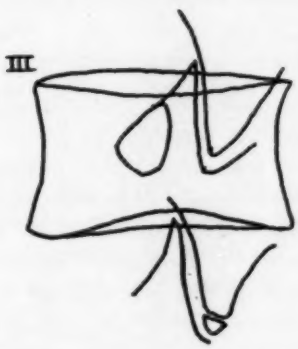

Fig. 6.—Diagram of the roentgenographic findings in case 2, right oblique view.

was no fracture but that the claimant had a congenital lesion of the spine. We therefore decided to give the patient the benefit of the doubt and reported the finding as ununited fractures of the lower articular processes of the third lumbar vertebra. We were not convinced, however, that we were dealing with fractures, but conceded that this may

have been another case of accessory articular processes, as described by Rendich and Westing. The case is therefore reported with the hope that it will stimulate further study of the problem. Rendich and Westing suggested that roentgenographs of the spine of applicants for hazardous positions in industry would prevent the physician's predicament in many doubtful cases of this sort.

After this report was prepared, one of us (W. K. K.) had the opportunity of seeing another case of formation of a gap through a lower articular process.

CASE 2.—J. L. R., aged 41, was being treated for a left ureteral stricture. Pyelographic examination was made on June 13, 1933. Except for slight hydronephrosis on the left side, the pyelograms did not show abnormalities. The roentgenograms, however, revealed a defect in the right lower articular process of the third lumbar vertebra. The gap was not transverse, as in the case reported earlier, but slightly oblique. The smaller fragment showed no atrophy or displacement. The edges of the bone at the gap were slightly denser than the rest of the bone. The spine was straight and did not show other anomalies. Another radiograph, taken according to Rendich and Westing's suggestion, with the patient rotated 45 degrees on the right side, plainly showed the small fragment of bone below the right lower articular process of the third lumbar vertebra. The patient could not remember having received an injury to the back or to any other part of the body. On specific questioning he did not complain of pain or discomfort. There was no limitation of motion in the spine.

Whereas there could be doubt in the first case as to whether we were dealing with a congenital malformation or with the result of an injury, there can be no doubt in the second case that we were confronted with a true case of an accessory articular process of the third lumbar vertebra.

SUMMARY

Two cases of formation of a gap through the lower articular processes of the third lumbar vertebra are reported.

In the first case there was a history of possible injury to the spine; therefore a question could be raised as to the correctness of the diagnosis.

In the second case there was no history of trauma, and there were no local symptoms; therefore the case is considered to be one of an accessory articular process of the third lumbar vertebra.

PERIPHERAL ARTERIAL THROMBOSIS

SECONDARY TO GONORRHEAL ARTHRITIS AND INTRAMUSCULAR INJECTION OF MILK

CHARLES H. MEAD, M.D.
DULUTH, MINN.
AND
ROLLA I. STEWART, M.D.
MINNEAPOLIS

Primary arterial thrombosis of nonembolic origin has been stated [1] to be unquestionably of bacterial origin. Only within the past thirty years, however, has much attention been directed toward, or any observation made of, thrombosis associated with infectious fevers. Arterial thrombosis is not considered to be unusual in cases of influenza, but in the other infectious diseases in which it has been encountered it is described as an uncommon complication. Welch [2] stated that arterial thrombosis associated with gonorrhea is very rare. Heller's [3] collection of only twenty-six instances from the literature illustrates its infrequency of occurrence.

Frazier [1] stated that chemical changes in the blood resulting in a liberation of fibrin ferment must be considered as an important etiologic factor in the production of arterial thrombosis. Welch stated that this factor is of undoubted importance, especially in thrombosis in toxic conditions. It is entirely conceivable that the intramuscular injection of milk or other foreign protein may act on the vascular system as a chemical etiologic factor. We failed, however, to find any record of intramuscular injection of milk resulting in peripheral arterial thrombosis.

Furthermore, it was stated [1] that there have been only a few cases of arterial thrombosis limited to, or terminating in, gangrene of the toes, although it is generally conceded that this lesion is more common in the lower than in the upper extremities. Associated gonorrhea and intramuscular injections of milk as unusual infectious and chemical etiologic

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1. Frazier, C. H.: Thrombosis and Embolism, in Keen, W. W.: Surgery, Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1916, vol. 1, p. 433.

2. Welch, W. H.: Thrombosis, in Allbutt, C., and Rolleston, H. D.: A System of Medicine, New York, The Macmillan Company, 1909, vol. 6, p. 691.

3. Heller, J.: Ueber Phlebitis gonnorrhoica, Berl. klin. Wchnschr. **41**:609, 1904.

factors in the production of peripheral arterial thrombotic gangrene, as well as the uncommon location of the resulting lesions, have been considered as justification for the report of the following case.

REPORT OF A CASE

The case is that of a white girl, 19 years of age, who was admitted to the Minneapolis General Hospital on Feb. 18, 1931, and discharged on June 8.

History.—The patient stated, on admission to the medical service, that five days previously malaise, chills and fever had suddenly developed. The onset of these symptoms was associated with a beginning menstrual period. One day later she noticed pain in the lower abdominal region and stiffness in both wrists and both knees. During the next three days the pain and stiffness spread to the back, ankles and left elbow. She was advised by her family physician to enter the hospital at this time.

The patient had contracted gonorrhea three years before the onset of the illness, and shortly afterward she had suffered from a mild attack of pelvic inflammatory disease. Vaginal smears had been positive for gonococci at that time. Treatment had been received until the smears were repeatedly negative.

Physical Examination.—Positive physical findings were limited to the abdomen, extremities and pelvis. Examination of the abdomen showed marked tenderness on palpation over both lower quadrants. No rebound tenderness was present. Moderate tenderness was present about the left elbow and knee, and there was marked tenderness about both ankles. There seemed to be some local heat in these regions, but neither swelling nor redness was noted. Pelvic examination showed a moderate fixation of the uterus and adnexa, with extreme tenderness on palpation or movement of these structures. Pelvic examination also intensified the diffuse pain in the lower abdominal region. The temperature ranged about 101 F., and the pulse rate was 95 beats per minute.

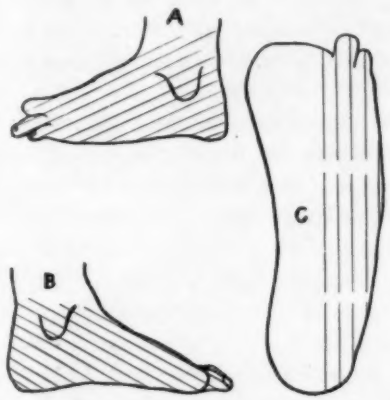
Laboratory Data.—The urine was normal. The blood showed 81 per cent hemoglobin and a white cell count of 15,700, 71 per cent of which were polymorphonuclear neutrophils. Repeated vaginal smears were negative for gonococci.

Diagnosis.—The clinical impressions were based on the past and present histories and the physical findings. It was concluded that the patient was suffering from gonorrheal arthritis of the left elbow, left knee and both ankles and chronic bilateral gonorrheal salpingitis.

Therapy.—The initial medical therapy consisted in the intramuscular injection of 60 cc. of defibrinated blood and the administration of salicylates in doses as large as the patient could tolerate. The symptoms remained unchanged, however, and the temperature continued to range about 101 F. Consequently, 8 cc. of milk was given intramuscularly on the suggestion of a dermatologic consultant. The temperature rose to 105 F.; the pulse became rapid, and the patient complained of great abdominal pain almost immediately after the injection of the foreign protein. Examination of the abdomen showed marked tenderness on palpation in both lower quadrants and definite rebound tenderness. Profuse perspiration, headache, backache, increased pain in the affected joints and leukocytosis were also noted. Swelling, redness, tenderness and local heat were noted in both lips and the left labium majus and on the dorsum of the left foot six days following the injection of milk. The latter symptoms rapidly disappeared, excepting in the left foot, where they subsided gradually. The tissues about the first, second and third toes then

became cold and numb. Later the foot became cold and cyanotic, and beginning gangrene was noted in the toes initially affected. There was now considerable pain in the foot and ankle. The gangrene became well demarcated at a much later date and involved only the first, second and third toes. There was associated superficial anesthesia over the dorsum of the foot to the level of the malleoli and along the lateral half of the sole. The patient was transferred to the surgical service on the development of well demarcated gangrene, and the toes involved were amputated.

Postoperative Course.—The patient's septic type of temperature had been slowly subsiding immediately preceding the amputation of the gangrenous toes. The temperature returned to normal following the operative procedure, and the patient was soon discharged from the hospital. The operative wounds healed satisfactorily, and the patient's general condition was much improved, but the areas of



A sketch illustrating the areas of superficial anesthesia on the left foot. *A* indicates the anesthetic area on the dorsum and the lateral aspect; *B*, the anesthetic area on the medial aspect, and *C*, the anesthetic areas on the sole.

superficial anesthesia persisted. The figure illustrates the areas of superficial anesthesia present at the time of discharge. The patient left the city shortly after discharge, and we were unable to follow the subsequent course.

COMMENT

The pathogenesis of thrombi is usually described as consisting of four factors: the presence of infective organisms, structural alterations of the intima, disturbances of the blood current and chemical changes in the blood.

It is with the infectious thrombi that the surgeon has to deal most frequently. The infectious diseases with which arterial thrombosis has previously been associated are influenza, typhoid fever, enteric fever, pneumonia, scarlet fever, typhus fever, tuberculosis, variola and the like. Streptococci have been the most frequently encountered offending

organisms. Singer,[4] however, considered the gonococcus as a possible etiologic factor as early as 1898, and the collected cases of Heller [3] substantiated his consideration. The case herein described would seem to be attributed to gonorrhea. However, this conclusion is based largely on circumstantial evidence, as positive findings of the gonococcus were not recorded from pelvic examination or examination of the blood stream or the affected joints during the patient's stay in the hospital. Some credence must be placed, however, on the fact that the patient had a positive smear for gonococci from the genital tract a short time previously; that pelvic examination showed an inflammatory disease process, and that the patient presented, in the minds of the attending internists, a clinical picture of gonorrheal arthritis. It is regrettable that no culture was made from the thrombi at the time of operation, but a negative result would not have eliminated gonorrhea as an etiologic factor, for in most cases bacteriologic examination of such thrombi has yielded negative results.

Structural alterations of the intima of the affected blood vessels as a result of the infectious disease may have been an etiologic factor. The action of infective agents in the causation of focal and diffuse diseases of the arteries has received considerable attention. The occurrence of acute and chronic arteritis as a result of various infective diseases, such as acute articular rheumatism, enteric fever, typhus fever, variola, scarlet fever, pneumonia, endocarditis, septicemia, syphilis, tuberculosis and leprosy is well established,[2] and it is not unreasonable to conclude that arterial thrombosis following gonorrhea may be referable to an infective arteritis. Other common causes of intimal changes would be unlikely in such localized areas of the vascular system and in a patient of this age.

Retardation of the blood current is but a predisposing or contributory cause, and consequently is of significance only when associated with a lesion of the vascular wall, the presence of organisms or chemical changes in the blood. The circulation in the lower extremities is relatively sluggish, and with evidence of an infectious process and possible chemical changes in the blood this factor may well have been contributory in the production of the lesions described.

That chemical changes in the blood are an etiologic factor in the production of such thrombi is as yet somewhat hypothetic. It is generally accepted that the use of foreign protein therapy is sound and productive of good results in many cases of gonorrheal arthritis and pelvic inflammatory disease. Schulman [5] enthusiastically recommended the intramuscular injection of milk as giving the most brilliant results in gonor-

4. Singer: Thrombose und Embolie im Wochenbett mit besonderer Berücksichtigung der gonorrhoischen Infection, Arch. f. Gynäk. **56**:218, 1898.

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rheal arthritis. Murray [6] stated that the great majority of workers have adopted sterile cow's milk as the agent of choice in the use of foreign protein therapy for pelvic inflammatory disease.

Neuhof and Hirschfield [7] showed, however, that the intravenous and intramuscular injection of sodium citrate, which is generally known as an anticoagulant, results in prompt and pronounced shortening of the coagulation and bleeding time. Salomon and Vey [8] also showed experimentally that the intravenous and intramuscular injection of various proteins and chemical agents results in a definitely decreased coagulation time. Conversely, Goldenberg and Panisset [9] injected milk intravenously into rabbits and mice, with no ill effects of any kind. The impression exists, however, that the reaction to many foreign proteins and chemicals injected intramuscularly is an increase in the coagulating power of the blood.

The reaction of the patient herein described to the injection of foreign protein was in no way unusual, the high temperature, leukocytosis, profuse perspiration, headache, backache, abdominal pain and increased pain in the affected joints being common immediate sequelae of this treatment. It is not difficult, however, to associate a possible chemical action on the blood with the other etiologic factors in the production of arterial thrombosis. At least the injection of milk was a potential etiologic factor in this case and clinically seemed to exert a potent influence in the production of the thrombotic lesions described.

SUMMARY

1. A case is reported in which a gonorrheal infectious process and the intramuscular injection of milk seem to be etiologic factors in the production of peripheral arterial thrombosis and gangrene in an unusual location.

2. Arterial thrombosis with resulting gangrene limited to the toes is a very uncommon occurrence.

3. Gonorrheal arthritis as an infectious etiologic factor in the production of arterial thrombosis is rare.

4. We failed to find a previous record of the intramuscular injection of milk as a probable etiologic factor in the production of peripheral arterial thrombosis.

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7. Neuhof, H., and Hirshfield, S.: The Intramuscular Administration of Sodium Citrate, a New Method for the Control of Bleeding, Ann. Surg. **76**:1, 1922.

8. Salomon, R., and Vey, E.: Der Einfluss von Proteinkörpern auf die Blutgerinnung, Arch. f. Gynäk. **116**:317, 1922.

9. Goldenberg, L., and Panisset, L.: Parenteral Injections of Milk, Paris méd. **2**:450 (Nov. 29) 1924.

INFLUENCE OF VENOUS STASIS ON HETEROTOPIC FORMATION OF BONE

NORMAN W. ROOME, M.D.
CHICAGO
AND
PAUL E. McMASTER, M.D.
LOS ANGELES

The question of the influence of circulatory changes on the healing of bone has been discussed by many authors with conflicting opinions. Pearse and Morton [1] and McMaster and Roome [2] have offered experimental evidence that the healing of defects of bones is accelerated by venous stasis. On the other hand, sympathectomy, with its increased flow of blood in the extremity, has been empirically advocated in the treatment of fractures by Leriche,[3] Colp and Mage [4] and others. Pearse and Morton,[5] Key and Moore [6] and McMaster and Roome [2] found no experimental confirmation of the value of such therapy. Clinically, certain atrophies of bone are explainable on the basis of arterial hyperemia (Greig [7]). Harris [8] listed several conditions known to cause hypertrophy and lengthening of the bones of children in which various degrees of venous stasis exist.

Formation of bone may be initiated by the transplantation of certain epitheliums into certain connective tissues. This effect was studied extensively by Huggins,[9] who found that bone occurred nearly con-

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From the Department of Surgery, the University of Chicago.

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2. McMaster, P. E., and Roome, N. W.: The Effect of Sympathectomy and of Venous Stasis on Bone Repair, J. Bone & Joint Surg. **16**:365, 1934.

3. Leriche, R.: Indications et resultats de la sympathectomie périartérielle dans la chirurgie des membres, Congres Français de Chirurgie, Paris, 1927, p. 435.

4. Colp, R., and Mage, S.: Experiences with Periarterial Sympathectomy in Fractures of the Lower Extremity, J. A. M. A. **97**:1069 (Oct. 10) 1931.

5. Pearse, H. E., and Morton, J. J.: The Influence of Alterations of the Circulation on the Repair of Bone, J. Bone & Joint Surg. **13**:68, 1931.

6. Key, J. A., and Moore, R. M.: Healing of Fractures, of Defects in Bone and of Defects in Cartilage After Sympathectomy, Arch. Surg. **26**:272 (Feb.) 1933.

7. Greig, D. M.: Clinical Observations on the Surgical Pathology of Bone, Edinburgh, Oliver & Boyd, 1931, p. 227.

8. Harris, R. I.: The Effect of Lumbar Sympathectomy on the Growth of Legs Shortened from Anterior Poliomyelitis, J. Bone & Joint Surg. **12**:859, 1930.

9. Huggins, C. B.: The Formation of Bone Under the Influence of Epithelium of the Urinary Tract, Arch. Surg. **22**:377 (March) 1931.

stantly in dogs on autotransplantation of the mucosa of the urinary bladder to the parietal fascias or muscles. A cyst forms by proliferation of the mucosa, and bone appears in relation to the newly formed mucous membrane from eleven to eighteen days after the transplantation (fig. 1). The experiments to be described are a study of the effects of venous stasis on such heterotopic deposits of bone.

Fig. 1.—Photomicrograph of bone formed by transplantation of mucosa of the urinary bladder into muscle planes; × 110. Note the bladder mucosa at *A* and the undecalcified bone at *B*.

EXPERIMENTAL METHODS

In each of six dogs, under morphine-ether anesthesia and with aseptic precautions, a small portion of the dome of the urinary bladder was excised and the defect closed. The mucosa was carefully dissected from the fragment, and two pieces, usually about 5 by 5 mm., of as nearly identical size and shape as possible, were sutured to the muscles of both hind legs beneath the deep fascia by fine inter-

rupted silk sutures. The right femoral vein and its four or five tributaries (saphenous, lateral circumflex, anterior femoral and muscular veins) in the upper part of the thigh were doubly ligated and portions excised. Roentgen studies were made at intervals. No suppuration occurred in any of the wounds, and no impairment of motion of the legs was noted. Five dogs died or were killed from twenty to three hundred and fifty days postoperatively; in three of these the cysts of the bladder mucosa and adjacent bone were excised en masse, the soft parts dissolved by boiling in a 1 per cent solution of sodium hydroxide for from thirty to sixty minutes, and the plaques of bone washed, dried and weighed. Dog 989 was kept, and the density of the transplant bone observed at intervals by means of roentgenograms for more than two and a half years.

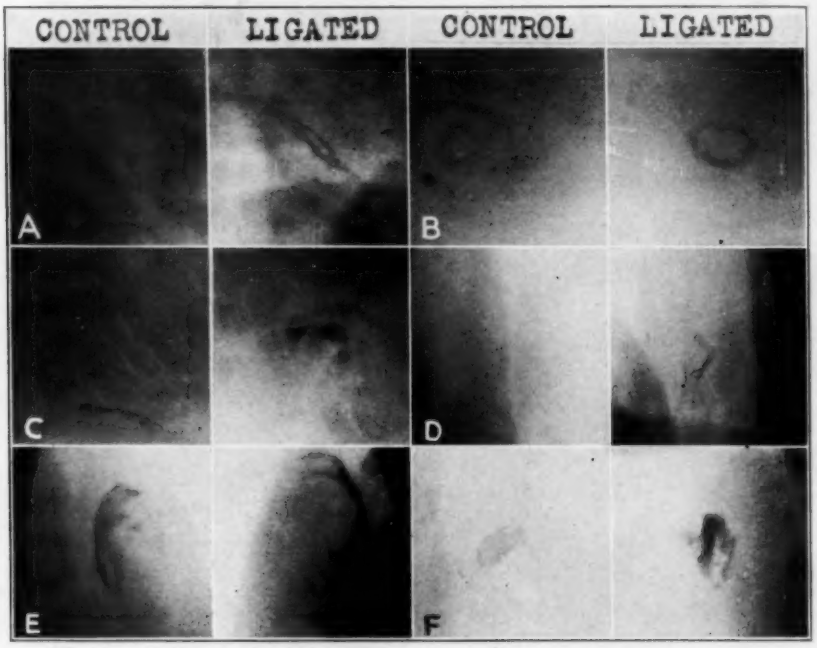

Fig. 2.—Roentgenograms showing the bone resulting from the mucosa transplantation of the bladder into the muscles of the leg: *A*, dog 173; *B*, dog 175; *C*, dog 283; *D*, dog 291; *E*, dog 927; *F*, dog 989. Note that in all films more dense bone is present on the side with venous ligations.

RESULTS OF EXPERIMENTS

By means of the roentgenograms, more dense formation of bone was observed in the leg with the ligated veins in five of the six animals (fig. 2). In one case (175) it was doubtful if there was any difference between the two sides in many of the roentgenograms.

In the cases in which the density of the bone was followed by roentgenograms over a long period, there was an increase in density for from one and a half to five and a half months, then a stationary

period followed by well marked diminution of the density of the bone, from four and a half to seven months postoperatively. Traces of bone persisted longer than two and a half years in the one dog studied over that period (fig. 3)..

Fig. 3 (dog 989).—Roentgenogram of transplanted bone at intervals, showing appearance at (*A*) twenty-one days, (*B*) thirty-five days, (*C*) one hundred and forty-five days and (*D*) four hundred and thirty-three days. Note the progressive increase in the density of the bone in the three upper films and the decreased density in the last film.

At necropsy on three of the animals (927, 173 and 175) there was definitely more bone recoverable from the ligated side in two cases and equal amounts in one case. The weights of bone obtained were as follows: dog 927, ligated leg, 157 mg., and control leg, 103 mg.; dog 173, ligated leg, 23 mg., and control leg, 1 mg.; dog 175, ligated leg, 21 mg., and control leg, 21 mg.

COMMENT

In spite of the obvious technical difficulty of transplanting exactly equal pieces of mucosa of the bladder into the legs of the dogs, it is thought that the consistent results obtained are significant, and that heterotopic formation of bone is accelerated by venous stasis. This conclusion is probably applicable to the general problem of the healing of defects of bone and fractures; i. e., that venous stasis promotes osteogenesis.

It is noteworthy that the bone formed in the soft parts by transplantation of mucosa of the bladder increases in density for a period, and then gradually atrophies. It thus behaves similarly to adult bone transplanted into the soft parts, as described by Phemister.[10] Traces of bone persisted longer than two and a half years, however, in the one dog studied over that period; the presence of the mucous membrane may be a factor in causing its persistence in the absence of stress and strain.

SUMMARY AND CONCLUSIONS

The effect of venous stasis on heterotopic formation of bone induced by transplanting similar portions of mucosa of the urinary bladder into the muscle planes of both hind legs, was studied in a series of six dogs. The femoral vein and its tributaries in the upper portion of the thigh were ligated and excised on one side, while the other leg was used as a control. It was found (1) that in five cases more bone was formed in the leg with venous ligations than in the control leg, while in one case the amounts were equal, as studied by roentgenograms and by weighing the bone plaques; and (2) that the bone formed about the transplant increased in density for a period of a few months, then atrophied, although the bone did not entirely disappear from the legs in the one case studied for two and a half years.

It was concluded that heterotopic formation of bone is accelerated by venous stasis.

5728 Drexel Avenue.

1930 Wilshire Boulevard.

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SUBCUTANEOUS BILATERAL SARCOID OF THE GLUTEAL REGION

REPORT OF A CASE

ALFRED KOERNER, M.D.

DAVID H. KLING, M.D.

AND

DAVID SASHIN, M.D.

NEW YORK

Among the many phenomena associated with arthritis and rheumatoid conditions nodular involvements of the skin compose an interesting group. Frequently some of the nodules resemble those seen in other conditions, so that the appearance of such masses is not always conclusive proof of a rheumatic etiology. Therefore, a careful differential diagnosis is essential.

REPORT OF CASE

History.—On March 14, 1932, a Jewish woman, aged 50, presented herself at Dr. Finkelstein's clinic. Four weeks before, while bathing, she discovered four lumps over the buttocks. The lumps were hard, painless and somewhat movable.

In 1928 a falling piece of ceiling struck the patient on the head. Examination at that time failed to reveal any injury. The pain disappeared after the application of an ice-bag. In 1929 she complained of a chronic cough and nervousness. At that time a few dry râles were heard in both lungs. Her blood pressure was 160 systolic and 100 diastolic, the urinalysis gave negative results and degeneration of the myocardium was diagnosed. Varicose veins were found, and for these she received four injections into the veins of the left leg, three of invert sugar and sodium chloride and one of sodium salicylate and sodium chloride. A severe reaction followed the last injection. The patient had two children and had had no miscarriages. The menopause set in at 42 years of age. With the exception of chronic constipation, she had had no other illnesses.

The husband had a right orchotomy for tuberculous epididymitis and at the time of his wife's examination was under treatment for a peripheral circulatory disturbance. The family history was otherwise irrelevant.

Examination.—The patient weighed 170 pounds (77.1 Kg.), was 5 feet 4 inches (162.6 cm.) tall, was somewhat pale and had false teeth. The throat and tonsils appeared normal. The internal organs gave no indication of a pathologic process. At the level of the third sacral vertebra, 1½ inches (3.77 cm.) from the midline, hard nodules could be palpated bilaterally which measured from 1 to 2 inches (2.5 to 5 cm.) in diameter. Two smaller lumps, each the size of a bean, were situated about 3 inches (about 7.5 cm.) from the midline. The masses were in the

Read before the Clinical Society of the Hospital for Joint Diseases, April 12, 1933.

subcutaneous tissue (fig. 1). The overlying skin was somewhat roughened. A Wassermann test was negative. A quantitative tuberculin test and a complement-fixation test for gonorrhea were negative; a sedimentation test was read as 17 per cent. A roentgenogram of both lungs showed a calcified nodule in the upper lobe of the left lung.

Biopsy.—On March 24, 1932, a specimen was removed for biopsy. Under procaine hydrochloride anesthesia, a slightly curved incision 3 inches (7.5 cm.) long was made over the left lower part of the back, along the upper fibers of the gluteus maximus muscle. On retracting the skin, a hard fibrous tumor, irregular in outline and infiltrative, was seen extending along the fascial plane, in places into the skin and in others toward the muscle. On attempting to excise the mass, a large number of vessels were encountered. A tumor about the size of a plum was removed and sent to the laboratory.

The microscopic examination was made by Dr. H. L. Jaffe, director of the laboratory, whose report follows: "Sections show very extensive single and conglomerate tubercles. There is no caseous necrosis. There is an extensive interstitial reaction in association with the inflammatory process. Tubercle bacilli will

Fig. 1.—On the left side the scar left following the biopsy can be seen, and on the right, ink markings indicating the nodules remaining.

be searched for in the section. I would suggest inoculating some of the material into a guinea-pig. The appearances are all in favor of the lesion being tuberculous. The exceptional possibility of its being syphilitic must be considered" (figs. 2 and 3).

Course.—The patient was discharged from the hospital on March 26. She came back to the clinic for dressings. On March 30, she complained of bleeding from the wound. A superficial slough developed, and the patient was readmitted to the hospital on April 4. The stitches were removed and a boric acid dressing was applied to the wound. Our diagnosis of possible sarcoid was then confirmed by Dr. Peck. The culture for tubercle bacilli and inoculation of guinea-pigs with secretion of the wound and tumor gave negative results. Sections stained for tubercle bacilli revealed none. Amyloid was absent on examination of specially stained sections made at the request of Dr. Gross, who also found in the nodules a resemblance to foreign body tumors. The wound healed under the dressings. The patient was discharged on April 13, but continued to receive injections of sodium cacodylate twice a week. Under this treatment the nodules on the right side diminished, until after eighteen injections, they were completely absorbed. The treatment was discontinued on July 6.

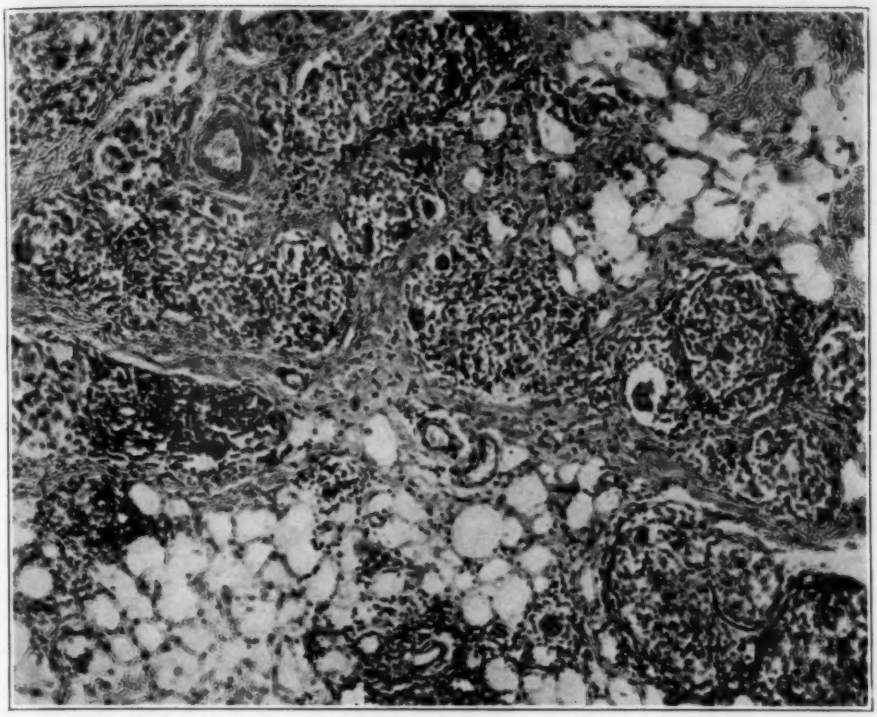

Fig. 2.—Low power magnification of a section of the nodule removed for biopsy, showing tubercles with giant cells divided off from one another by septums of connective tissue and numerous lymphocytes.

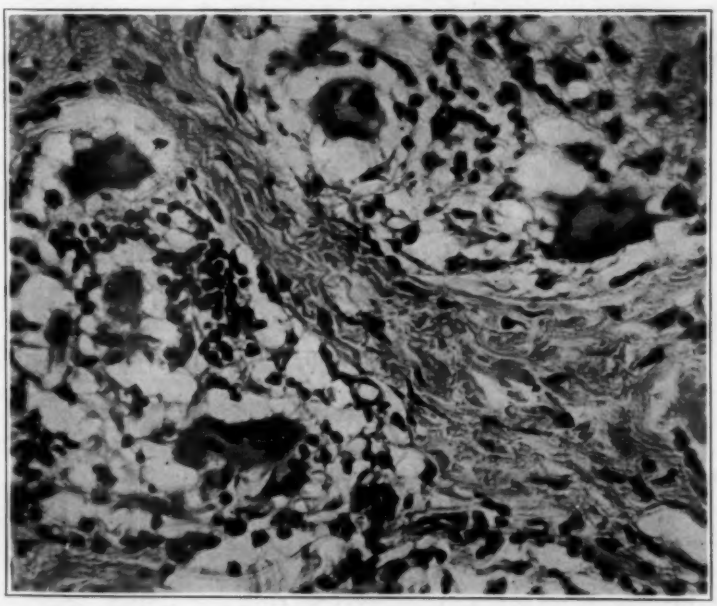

Fig. 3.—High power magnification of a section of a tubercle showing giant cells.

Reexamination.—On Jan. 23, 1933, a review of the patient's condition showed a firm scar in the left gluteal region. All the nodules had been absorbed completely. A slight amount of atrophy of the overlying skin and brownish pigmentation were still present.

After Boeck [1] in 1899 designated the name "sarcoid" for certain tumors, Fendt [2] defined it as signifying a circumscribed benign tumor of limited growth composed of groups of round cells, divided off in its substance by septums, but as a whole encapsulated and frequently healing in response to treatment with arsenic. Many examples of the condition were found and described, but it was not until 1910 that Darier [3] brought forth the first comprehensive and satisfying classification.

He grouped all cases into four sections: (1) multiple benign sarcoid of Boeck; (2) subcutaneous type, of Darier-Roussy; [4] (3) erythema induratum of the extremities; (4) Spiegler-Fendt [5] type, a nontuberculous nodule composed of round cells, resembling the condition known as leukemia cutis or lymphodermia.

The case described here belongs to the Darier-Roussy group. Generally speaking, tumors in this group are subcutaneous, round or oval, the size of a walnut and painless. They occur on the trunk, especially on the upper part, or on the side of the abdomen. They seldom ulcerate, and there is usually a negative reaction to tuberculin. Histologically the nodules are composed of epithelioid and giant cells, mostly of the sarcoma type, although occasionally of the true Langhans type with lymphatic infiltration about the epithelioid layer. The nodules may occur in chains along the blood vessels.

Kuznitsky [6] described cases in which the cutaneous manifestations were coupled with a similar involvement of the internal organs, including the liver, spleen, lungs, lymph glands and kidneys. He considered the disease systemic rather than cutaneous.

A number of conditions must be differentiated from sarcoid, including among others myogelosis, subcutaneous rheumatic nodules, tuberculosis cutis, gumma, metastatic tumors, inflammatory reactions around sites of injections and aberrant glands.

Etiologically, sarcoid has been much in doubt, Boeck claiming it to be tuberculous, Pautrier [7] syphilitic and others infectious but of unde-

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1. Boeck: J. Cutan. Dis. **17**:543, 1899.
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3. Darier: Monatsh. f. prakt. Dermat. **50**:419, 1910.
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5. Spiegler: Arch. f. Dermat. u. Syph. **27**:163, 1894.
6. Kuznitsky: München. med. Wchnschr. **62**:1349, 1915.
7. Stillians, A. W.: J. A. M. A. **77**:1615 (Nov. 19) 1921.

termined cause. Kyrle [8] found tubercle bacilli in the lesions as early as ten days after their onset, yet was not able to demonstrate them in specimens from the same lesion at thirty-six days, while Pautrier found syphilis associated with sarcoid of the Boeck type and also with that of the Darier-Roussy type. In the exceptional cases observed by Pautrier, cure was accomplished by antisyphilitic treatment. Thereafter he was of the belief that the condition was as closely related to syphilis as to tuberculosis. Stillians,[7] in 1921, concluded as a result of his work on the subject that neither of the two types so treated by Pautrier was ever caused by Spirochaeta pallida, but that the erythema induratum type may sometimes be so caused.

Prognosis in cases of sarcoid must be guarded as to the disappearance of the nodules, but may be good as to survival.

The treatment, in addition to that mentioned, has in some cases included use of endothermy, mercurous chloride, tuberculin and roentgen rays. Atrophy and slight pigmentation usually follow the absorption and disappearance of the nodules.

SUMMARY

A subcutaneous tumor of the physical attributes seen in this case, not associated with rheumatic involvements, associated with negative reactions to the Wassermann test and to the various tests employed with and diagnostic of tuberculosis, uncomplicated by any phenomenon of metastasis, not involving the general health, shown by biopsy to have a definite and characteristic histologic structure, not ulcerating and responding typically to arsenical medication, can by these criteria be safely designated as a true sarcoid tumor of the Darier-Roussy type.

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INFLUENCE OF BLADDER TRANSPLANTS ON THE HEALING OF DEFECTS OF BONE

GLOVER H. COPHER, M.D.
AND
J. ALBERT KEY, M.D.
ST. LOUIS

Having been interested in the problem of osteogenesis and the healing of bone we were attracted by the work of Huggins,[1] who showed that if the mucous membrane of the bladder was transplanted to the subcutaneous tissue of dogs the transplant tended to produce a cyst lined by bladder epithelium, and true bone tended to be formed in the wall of the cyst. It occurred to us that epithelium from the bladder might stimulate osteogenesis in defects in bone and cause union to occur in defects which would normally result in nonunion. In this article we report experiments in which relatively large defects in bone in the ulnas of dogs were bridged by transplants of the mucous membrane of the bladder of the same animal.

REVIEW OF THE LITERATURE

The literature on heteroplastic formation of bone and especially on formation of bone in the genito-urinary tract has been reviewed by Huggins,[1] so that it will not be necessary to repeat it here. Neuhof [2] noted that if fascia was transplanted into defects in the urinary bladders of dogs, bone constantly developed on the surface of the fascia which was adjacent to the bladder cavity, and that the bone was invariably confined to the transplanted fascia. He believed that the bone was formed by metaplasia of the tissue and that the metaplasia was caused by the deposition of lime salts in the necrotic tissue of the fascial patch which was in contact with the urine. It was his belief that the imbibition of calcium salts acted as a stimulus to the surrounding connective tissue which caused it to build up as powerful a barrier as possible, namely, bone.

Neuhof's experiment was repeated, and the observation on the formation of bone was confirmed by Phemister.[3] Phemister noted that while

From the Department of Surgery, Washington University Medical School.

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bone was formed in the fascial patch in the dog, it was not formed in similar transplants in the bladders of rabbits and sheep. He believed that this was due to the fact that in dogs the urine is acid in reaction while in herbivorous animals it is alkaline, and he believed that the acid reaction had something to do with the formation of bone.

Huggins [1] transplanted mucous membrane from the bladder into various tissues, and showed that if a strip of the mucous membrane of the bladder was transplanted to the rectus sheath, fascia lata, subcutaneous tissues or muscle of the dog, true bone developed in the transplant and that this bone contained haversian canals and hematopoietic marrow. The bone was always produced in the wall of the cyst and appeared to be formed under the influence of the proliferating cells lining the cyst. Huggins and Compere [4] showed that in the majority of instances the fluid contained in these cysts was unusually high in calcium and phosphorus as compared with the blood of the same animal. This capacity to stimulate formation of bone was apparently specific for the bladder since bone did not occur in transplants of other epithelial tissues (from the gallbladder or gastric, jejunal and prostatic epithelium). Furthermore, the bladder transplants seemed to require a certain type of fibrous tissue for formation of bone, as no bone was formed when bladder mucosa was transplanted into the kidney, liver or spleen.

MATERIALS AND METHOD

This report is based on the results obtained from operations on twenty-four adult dogs. The operative procedure was as follows:

Under ether anesthesia the hair was removed from the abdomen and forelegs. The skin was prepared for operation with iodine. The urinary bladder was exposed and a piece of the wall of the bladder, approximately 2 cm. square, was excised. The defect in the bladder was sutured, and the abdominal wound was closed. The mucous membrane from the bladder was then dissected from the muscularis and was divided into two equal portions. The lower third of the ulna of each leg was exposed, and approximately 1 cm. of the shaft was resected subperiosteally. Such a large defect will usually result in nonunion. On the right side, one of the pieces of mucous membrane from the bladder was sewed into the defect of the ulna, while the left side was kept as a control. The wounds in the two legs were then closed in layers. Through a separate incision in the abdominal wall, the other half of the mucous membrane from the bladder was spread out on the deep fascia of the abdominal wall and was sutured in place, after which the wound was closed. The dogs were killed at intervals of from seven days to nine months. The specimens were examined in the gross; then, after roentgenograms had been made they were fixed, decalcified, sectioned, stained and studied microscopically.

4. Huggins, C. B., and Compere, E. L.: Calcium and Phosphorus Content of Epithelial Lined Cysts from Transplantation of Mucosa of Urinary Bladder to Rectus Sheath in Dogs, Proc. Soc. Exper. Biol. & Med. **27**:753 (May) 1930.

In addition to the experiments just described, ten experiments were performed in which the bladder was opened and some of the epithelium was scraped off the surface. These scrapings were transplanted into defects in the right ulna of the same animal, while a similar defect was made in the left ulna for a control.

RESULTS

The results of the longer experiments are shown in the table. Union occurred on the control side (left) in only two instances.

In the right leg, in which the defect in the bone was bridged by a strip of bladder mucosa, union by bone occurred nine times; new bone was formed in the defect in every case, and in thirteen of the sixteen experiments the production of bone was marked. Not only was new bone produced in the defect, but union was the rule, and even in cases in

Results of Transplanting Mucous Membrane from the Bladder to Resected Right Ulnas of Dogs *

Dog	Time, Days	New Bone		Union		Atrophy	
		Right	Left	Right	Left	Right	Left
355	35	+++	0	+	—	—	+
B33	49	+++	+	—	—	—	+
B6	49	++	—	+	—	—	+
400	52	++	—	+	—	—	+
B40	57	+++	—	—	—	—	+
B42	59	+++	—	+	—	—	+
B54	59	++++	—	+	—	—	+
A19	60	++++	++	+	—	—	+
B20	71	+++	—	—	—	—	+
352	73	++++	—	+	—	—	+
S41	75	++	—	—	—	—	+
A9	90	+++	—	+	—	—	+
B43	99	++++	—	+	—	—	+
353	217	++++	++++	+	+	—	—
A16	270	++++	++++	+	+	—	—
166	270	++++	—	+	—	—	+

* The left ulna is the control.

which union by bone did not occur, the atrophy which was uniformly present in the control experiments (with nonunion) was not present on the side which contained the bladder transplant.

Gross Appearance.—In the experiments of short duration there was little difference between the control and the defect which was bridged by the bladder transplant except that the callus tended to be more voluminous and more firm on the side with the transplant. This callus contained cysts which varied in size directly as the duration of the experiment. In experiments of long duration, in which the control sides did not unite by bone, the ends of the fragments were reduced in diameter, were atrophic in appearance, and the defect was bridged by a strand of dense fibrous tissue. In the same animals the ulnar defects which had been bridged by bladder mucosa presented very different pictures. Here the ends of the bones were usually enlarged and rather more dense than normal, and the defect was filled by a mass of tissue

which consisted of either callus or bone and which contained cysts, varying in size directly as the duration of the experiment. In some of the longer experiments these cysts were quite large and projected from the side of the bone, the largest individual cyst, which measured 2 by 1.5 by 1 cm., being produced in the experiment which lasted for two hundred and seventeen days. In practically every instance these cysts were multilocular, or else multiple small cysts were present.

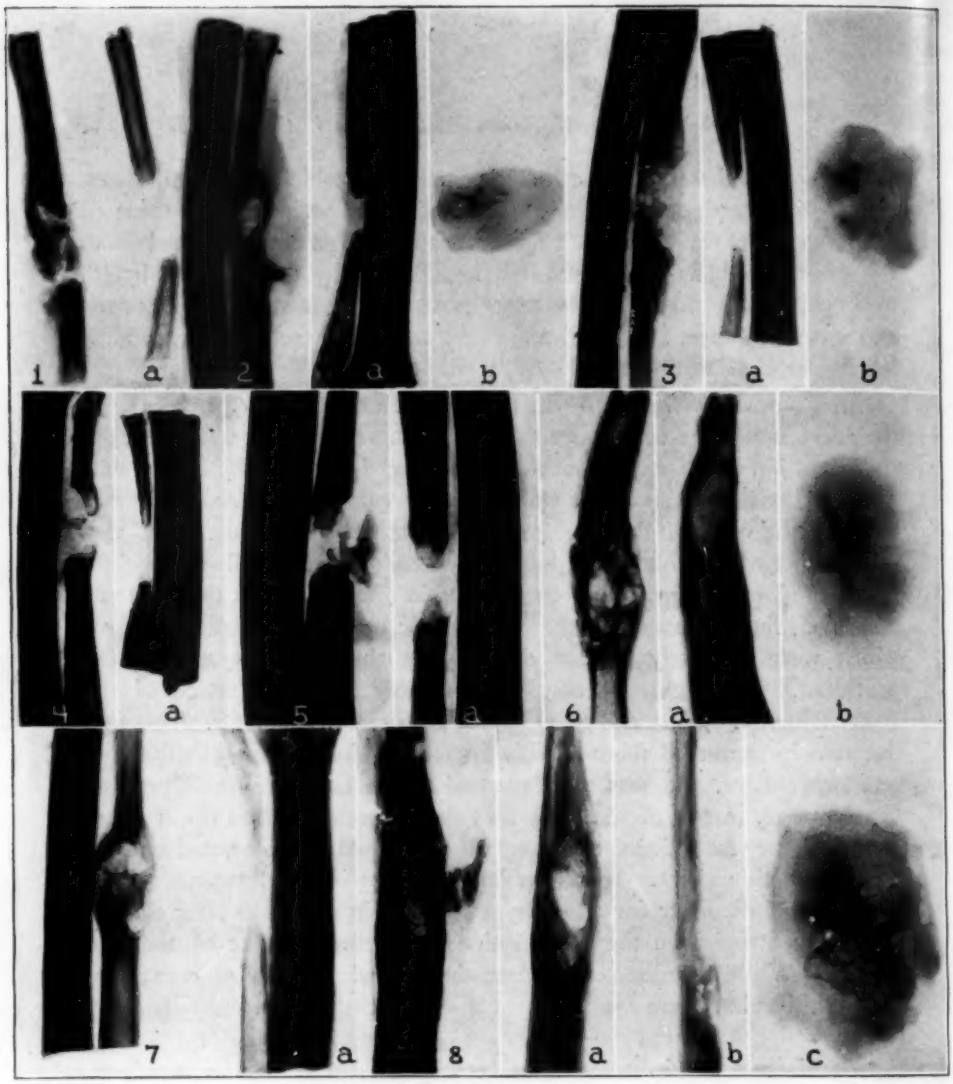
Roentgen Examination.—In the seven and fifteen day experiments the roentgenograms of the transplant and control sides were practically the same, but in the experiments which lasted from three to four weeks the roentgenograms showed a thin strand of calcified material stretching between the ends of the bone on the transplant side, while there was no evidence of new bone bridging the defects on the control sides.

In the longer experiments the defects in the control not only showed nonunion, but the bones on the control side exhibited atrophic changes which were definitely present as early as thirty-five days after the operation. These changes consisted not only of a rarefaction of the ends of the bones, but also of a definite decrease in diameter. Although the atrophy occurred more rapidly in some animals than in others, it was progressive, and was most marked at the ends of the fragments. For instance, in one of the forty-nine day experiments the upper fragment of bone was reduced to about half its normal diameter, and tapered down to a thin point. In others the bones maintained approximately their normal diameter for a longer period, but in all of the later experiments the atrophy on the control side was definite. One of the two instances in which union occurred on the control side was an exception, and in this ulna there was little or no demonstrable atrophy (figs. 1 to 8).

The defects which had been bridged by the bladder transplants presented a different appearance, for in all of these in which the experiment lasted over thirty-five days the ends of the fragments retained their normal size and density or were unusually large and more dense than normal. Not only was there no atrophy, but union by bone occurred in twelve of the sixteen experiments (table and figs. 1, 3, 6, 7 and 8).

In the four instances in which union by bone failed to occur on the side with the transplant, not only was there no atrophy, but considerable new bone was produced in the defect (figs. 2, 4 and 5).

Of the two cases of union on the control side one occurred in the seven month, and the other in a nine month, experiment (figs. 6 and 8). In the seven month experiment the control side showed union, with reestablishment of the medullary cavity (fig. 6). These two experiments also showed the type of union produced by the bladder transplant; that is, the bone became enlarged, the ends of the fragments became



Figs. 1 to 8.—Roentgenograms showing: defects of bone in the ulna bridged by transplants of bladder mucosa; defects in the control in the opposite ulna; four cysts formed by bladder transplants in the abdominal wall. 1. Bladder transplant after thirty-five days; *a*, control. 2. Bladder transplant after fifty-nine days; *a*, control; *b*, cyst in the abdominal wall. Note in figure 2 two spicules of new bone attached to the distal fragment, but not united by bone to the proximal fragment. These were separated by a cyst. There is a small stellate mass of bone in the cyst in the abdominal wall. 3. Bladder transplant after fifty-nine days; the defect is bridged by a mass of bone which contains numerous small cysts, causing it to have a worm-eaten appearance; *a*, control; *b*, a cyst in the abdominal wall. 4. Bladder transplant after seventy-five days; the defect is occupied by two large cysts resulting in nonunion; *a*, control. 5. Bladder transplant after seventy-five days; there is nonunion on both sides, but on the side of the bladder transplant there is a considerable amount of new bone attached to the lower fragment, the defect being occupied by cysts; *a*, control. 6. Bladder transplant after two hundred and ten days; *a*, control with union; *b*, cyst in the abdominal wall. 7. Bladder transplant after two hundred and seventy days; note the multiple cysts in the bone bridging the defect on the side with the transplant; *a*, control. 8. Bladder transplant after two hundred and seventy days; note the cavity in the bone on the side with the transplant and the spicule of new bone projecting from the side of the ulna; *a*, lighter print to show a cyst in the bone; *b*, control, showing union; *c*, cyst in the abdominal wall.

eburnated, and the defect was occupied by a mass of tissue containing bone and many clear areas. These clear areas represented multiple cysts. In addition to the cysts in the bone there were, in these two instances, large cysts projecting from the sides of the bone at the site of the preexisting defect.

A good example of the end-result in the defects in the transplant and control is shown in the specimen from the experiment lasting two hundred and seventy days (fig. 7). Here the multiple cysts possessed a dense fibrous wall on their free surfaces and contained a thin brownish fluid. Occasionally part of the wall of the cyst projecting from the shaft of the ulna contained considerable bone, as illustrated in figure 8.

Abdominal Transplants.—All of the abdominal transplants produced cysts which varied in size directly as the duration of the experiment, the smallest appearing in the earlier experiments and the largest, measuring 4.5 by 2.5 cm., occurring in a nine month experiment. All of the cysts contained a thin brownish fluid and all possessed a base of dense connective tissue and a dense fibrous wall, which composed the dome of the cyst. In all except the first two transplants, definite bone was produced, and this bone was always present in the base of dense connective tissue and never in the dome of thin connective tissue.

In the microscopic sections bone was seen in the wall of the abdominal cyst of the twenty-one day experiment. However, in eight of the twenty experiments which lasted thirty-five days and longer, the bone was so small in amount that it was not demonstrated in the roentgenograms of the cysts.

The amount of bone produced in the walls of the abdominal cysts was not as great as the amount of bone produced around similar transplants of mucous membrane from the bladder which were placed across a fresh defect in the ulnas of the same animals (figs. 2, 3, 6 and 8).

Microscopic Examination.—Controls: In the controls, the defect in the early experiments was filled with a mass of blood clot and granulation tissue, and there was some proliferation of osteogenic tissue from the ends of the fragments and beneath the periosteum. There was no tendency to form a strip of new bone along the periosteum which bridged the defect. The subperiosteal new bone projected only a short distance beyond the ends of the fragments and tended to dip into the defect and become continuous with the new bone springing from the osteogenic tissue in the medullary cavity, thus forming a sort of end-bulb of callus and new bone. However, instead of the formation of new bone progressing and tending to fill the defect, the process ceased in a short time and the new bone was absorbed, and the defect became filled with fibrous tissue while the ends of the fragments atrophied.

In a specimen examined thirty-five days after the operation the defect on the control side was filled with a mass of fibrous tissue, and the ends of the fragments were markedly atrophied, the atrophy apparently being due to large numbers of osteoclasts eroding the bone at the ends and around the circumference of the fragments beneath the periosteum. This osteoclastic absorption continued throughout the experiments and must sometimes have been present simultaneously with a small amount of formation of new bone, since in most of the controls there was evidence of osteoclastic resorption as well as formation of new bone around the ends of the fragments. Osteoclastic resorption was present even in the longer experiments, but with the bones very

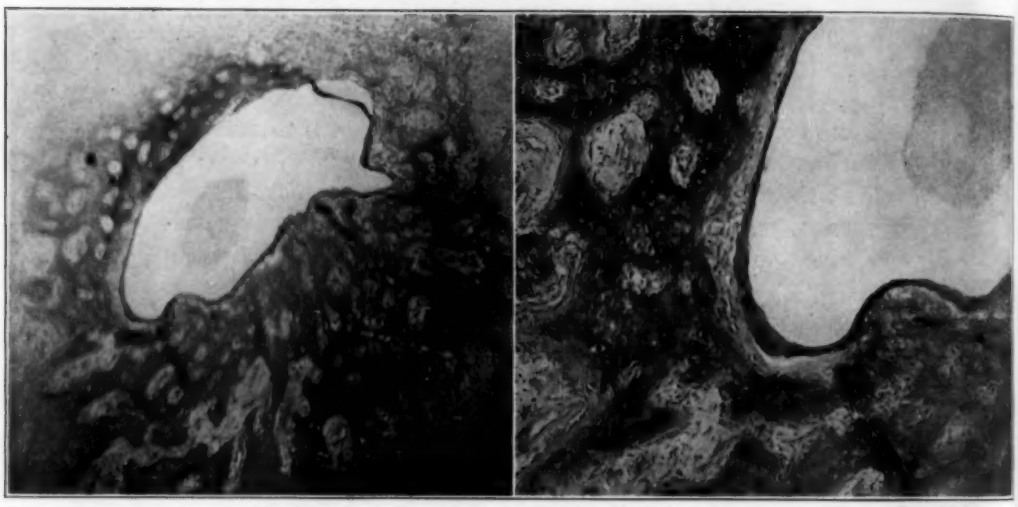


Fig. 9.—Fifteen day experiment: This shows a portion of a small cyst in the defect on the side of the bladder transplant with new bone around the cyst; 32 mm. objective on the left and 16 mm. on the right.

atrophic, the number of osteoclasts was considerably less than in the earlier experiments in which the resorptive process seemed to be more active.

Bladder Transplants in the Ulna: In the seven day experiment the defect in the ulna was filled with an organizing blood clot containing masses of bladder epithelium, in some of which the cells had proliferated. In the experiment using the scrapings these cells had formed small cysts. Some of the cysts contained a granular precipitate while others contained small spherules, most of which could be stained with eosin. There was no evidence of bone around the walls of the cysts. The ends of the fragments of bone were apparently dead, as the lacunae were empty, but there was rather marked proliferation of osteogenic

tissue beneath the periosteum and around the ends of the bones, with the formation of some callus and new bone. There was a short finger-like mass of new bone extending out from the medullary canal of the end of one fragment (endosteal bone).

In the fifteen day experiment the blood clot had largely disappeared and the defect was filled with young connective tissue which contained two rather large masses of cartilage. In the center of one of these was

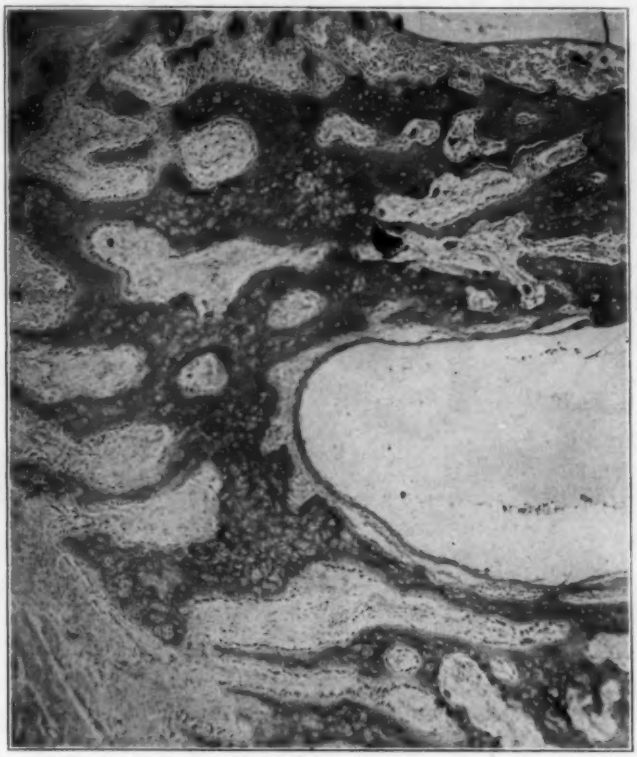


Fig. 10.—Twenty-one day experiment: New bone around the margin of the cyst is lined by bladder epithelium which spans the fragments; 16 mm. objective.

a small cyst lined by bladder epithelium, and around the wall of the cyst was a thick layer of newly formed cancellous bone (fig. 9). Some of this bone merged into the surrounding cartilage and appeared to have been formed by calcification of the cartilage, while in other areas in the same mass the bone apparently had been formed by osteogenic cells in a matrix of connective tissue, showing no evidence of a cartilaginous stage. In most places the epithelium of the wall of the cyst was separated from the surrounding bone by a thin layer of connective tissue or by a homogeneous hyaline layer. Osteogenesis appeared to be

proceeding from the wall of the cyst outward. In another fifteen day experiment in which a strip of membrane was used, a large cyst extended almost across the defect, and some new bone was present along the wall of the cyst next to the callus in the defect.

The ends of the bones in the fifteen day experiment were covered by a cap of new bone, some of the trabeculae of which were continuous with the necrotic ends of the fragments. There was considerably more new bone here than in the experiments lasting seven days.

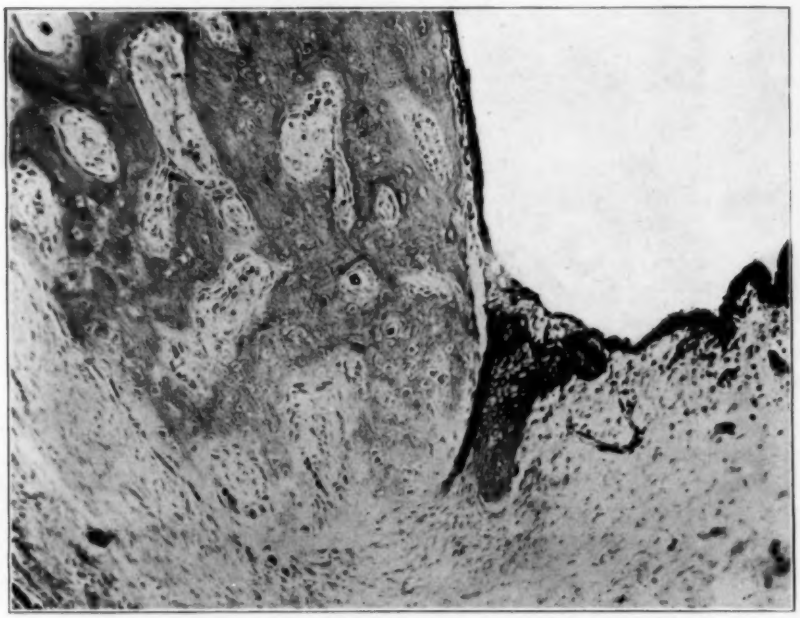


Fig. 11.—Twenty-one day experiment: Note the margin of new bone along one wall of the large cyst lined by bladder epithelium; 16 mm. objective.

In the twenty-one day experiment the defect was spanned by a large cyst, one wall of which was bounded by a thick layer of new bone which was continuous with the subperiosteal new bone around the end of one of the fragments (figs. 10 and 11).

In the longer experiments there was a progressive increase in the amount of callus and bone between the fragments and also a progressive increase in the amount of bladder tissue. The callus tended eventually to span the defect and then to undergo a transformation from an embryonic type to the adult type of bone (fig. 12). In many instances small masses of bladder tissue became incorporated in the callus and formed thin-walled cysts surrounded by bone. In other instances the bladder transplant formed one or more large cysts which often lay along the new

bone which spanned the defect. In the older experiments these cysts were lined by a thin layer of atrophic epithelium, and the walls consisted of a dense collagenic layer which contained very few cells.

It was not possible from a study of the sections of the longer experiments to draw any conclusions in regard to the influence of the bladder transplants on the formation of new bone, as there was no constant relation between the new bone and the bladder transplants. In some sections much new bone was present in areas in which no bladder tissue was seen, while in other sections, or even in other areas of the same section, the new bone was laid down along the cyst wall, or the

Fig. 12.—Fifty-nine day experiment: The cyst is lined by several layers of bladder epithelium with mature bone adjacent to the wall of the cyst; 8 mm. objective.

bladder epithelium was closely applied to a mass of bone, with only a thin basement layer intervening. In some of the older experiments the defect was bridged by a mass of adult bone which contained numerous small cysts lined by bladder epithelium (fig. 13). It was especially noticeable that atrophy of bone did not occur in the presence of the bladder transplants, and that the ends of the fragments tended to remain intact and maintain their normal density or become more dense than normal.

Abdominal Transplants: There was marked proliferation of the bladder epithelium and beginning formation of cysts in the seven day specimens. In the fifteen day specimens small cysts had been formed.

and in the twenty-one day specimens the cysts had reached a diameter of 7 mm. The earliest new bone was found in the twenty-eight day specimen. This consisted of several small patches of ossification in the fibrous tissue of the wall of the cyst. Apparently this bone was formed in connective tissue without any preceding formation of cartilage. In all of the older cysts a variable amount of bone was present in the connective tissue adjacent to the walls of the cysts. In some instances this bone formed large plaques, and in others the cysts were surrounded by a shell of bone, or the bone around several cysts had

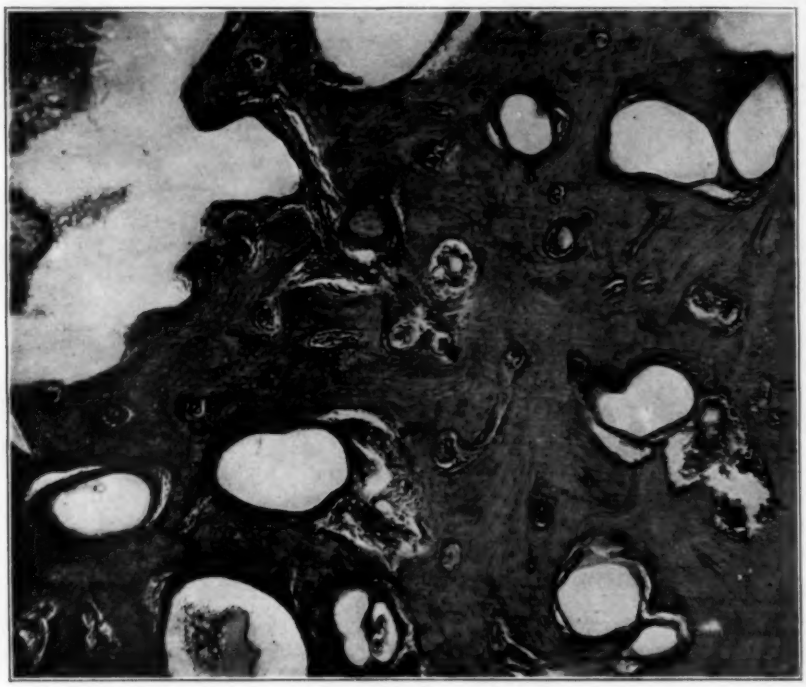


Fig. 13.—Two hundred and seventy day experiment: A portion of a large cyst can be seen in the upper left-hand corner and multiple small cysts scattered through the mature bone which is bridging the defect; 16 mm. objective.

coalesced to form a mass from which the cysts protruded. Hyaline cartilage was occasionally seen in the bone in some of the later cysts, but in no instance was there any indication that cartilage was formed earlier than bone.

COMMENT

The results of the experiments reported in this paper indicate that the presence of a growing transplant of epithelium from the bladder tends to stimulate osteogenesis in the defect and causes it to be bridged by new bone in circumstances which would ordinarily result in nonunion.

Microscopic examination of specimens removed from one to four weeks after the operation indicated that the new bone was formed directly under the influence of the growing epithelium of the bladder and was not the result of formation of bone along a strip or sleeve of periosteum bridging the defect. This statement is based on the observation that in the early experiments the new bone usually lay close to the proliferating epithelium and bore no constant relation to the periosteum.

We shall not attempt to settle the question as to whether or not periosteum can be depended on to form bone, as our operations were not executed carefully enough to be of value in this respect. We simply exposed the ulna, split the periosteum, pushed it back with an elevator and removed a section of the shaft—an operation which we would expect to result in nonunion. In young animals a fairly complete sleeve of periosteum was left, but in old animals the periosteum was thin and tore easily, so that no such sleeve was obtained. However, even in old animals there was always a strip of intact periosteum left along the interosseus membrane, so that in all of our experiments the defect was bridged by periosteum. An effort was made to make the control defect in the left ulna as nearly like that in the right ulna as possible.

No effort was made to determine how wide a defect could be bridged by bone under the influence of the bladder transplant. In fact, our effort was to make the defects just wide enough to assure nonunion, and in two instances we failed to do this as is indicated by the fact that union occurred on the control side (figs. 6 and 8). However, the fact that nonunion resulted in fourteen of sixteen controls in which the experiments lasted over thirty-five days is evidence that in the main our defects were adequate, and the observations on formation of new bone and union in the right ulna as recorded in the table are evidence that the bladder transplant in these limbs exerted an influence on the formation of new bone in the defect.

Not only did the bladder transplant cause new bone to form in the defect, but it also tended to prevent the atrophy of the ends of the fragments which uniformly occurred on the control side with nonunion. This was true even in the four instances in which union did not occur on the side with the transplant.

The presence of the transplant in the vicinity of a fracture appeared to result in the production of a larger amount of bone than occurred in similar transplants of bladder epithelium in the abdominal wall. Not only this, but the bone appeared earlier (after fifteen days in the defects and after twenty-eight days in the cysts in the abdominal wall). This was partly due to the fact that some osteogenesis was caused by the fracture, but experiments in progress indicate that the presence of a

reservoir of calcium in the vicinity of a bladder transplant in the abdominal wall results in the production of more bone in the wall of the cyst than occurs in a similar transplant which is not close to a calcium depot.

We are not yet able to explain the mechanism by which the bladder transplant causes formation of bone. As we have already stated, the bone was usually formed directly in the connective tissue and was not preceded by the formation of cartilage. It is possible that the bone is due to the presence of a local excess of calcium, and that this calcium is secreted by the epithelial cells of the transplant. This theory is in accord with the observations of Huggins,[1] who noted that the fluid in the cysts contained a higher concentration of calcium than did the blood of the same animal.

We have considered the possibility that the bladder epithelium might contain some substance which tends to cause formation of bone. Working on this hypothesis we have made various kinds of extracts of bladder epithelium and injected them into the tissues around experimental fractures, but thus far the results of these experiments have been negative.[5]

CONCLUSIONS

Homologous transplants of epithelium from the urinary bladder tend to cause formation of bone in their vicinity, and if they are placed in a defect of bone they tend to cause union in defects which would ordinarily result in nonunion.

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ACANTHOMA OF THE ANUS

REPORT OF THREE CASES

FRANKLYN D. HANKINS, M.D.

AND

WARREN G. HARDING, 2D, M.D.

LOS ANGELES

The occurrence of an acanthoma at the anus is sufficiently rare that few observers are privileged to study more than 1 case. In a study of 1,097 cases of malignant tumor occurring in 9,000 consecutive autopsies performed in the Los Angeles County General Hospital, we have had the opportunity to study 3 cases of epidermoid carcinoma which arose in the anorectal region. This constituted an incidence of 1 per cent of all the primary new growths found in the gastro-intestinal tract, and approximately 3 per cent of the carcinomas arising in the large bowel. Lynch [1] in a review of 491 cases of cancer of the rectum and pelvic colon reported 15 cases of epithelioma, an incidence of 3 per cent. Pack,[2] after an extensive study of anal and rectal neoplasia, concluded that epithelioma in this region was comparatively rare, with an incidence of from 3 to 4 per cent. Brofeldt [3] studied 260 cases of rectal tumors and reported 5 cases of squamous cell carcinoma, 2 of which were not verified by microscopic study. The cases reported in our study occurred in a series of 46 malignant tumors originating in the anorectal region,[4] thus giving an incidence somewhat higher than that reported by other observers.

The literature of the past two decades contains reports of 40 cases of anal acanthoma. Kerr,[5] in 1913, reported the successful resection of a cauliflower-like mass arising at the anal mucocutaneous junction which proved histologically to be an epidermoid carcinoma. Lynch,[1] in 1917, reported 15 cases of anal epithelioma without attempting to

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From the Department of Pathology (Dr. Newton Evans, Director), Los Angeles County General Hospital.

1. Lynch, Jerome M.: Cancer of the Rectum and Pelvic Colon, J. A. M. A. **69**:1775 (Nov. 24) 1917.

2. Pack, George T.: The Pathological Aspects of Anal and Rectal Neoplasia, Internat. Clin. **2**:77 (June) 1927.

3. Brofeldt, S. A.: Zur Pathogenese des Plattenepithelkrebses der Pars analis recti, Acta Soc. med. fenn. duodecim **8**:3, 1927.

4. Harding, Warren G., 2d, and Hankins, Franklyn D.: Post Mortem Observations of 118 Carcinomas of the Large Bowel, Am. J. Cancer **17**:634 (Feb.) 1933.

5. Kerr, H. H.: Epithelioma of the Anus, Surg., Gynec. & Obst. **16**:108 (Jan.) 1913.

describe the clinical course or the pathologic findings in the disease. In a case of squamous cell carcinoma of the anus roentgen therapy was used by Lockhart-Mummery [6] in 1923. One such tumor, arising at the site of an imperforate anus, was described by Mecray [7] in 1926. Wallon,[8] Hawe [9] and Plisson [10] reported cases in 1927. In addition Brofeldt [3] reviewed the pathogenesis of pavement cell carcinoma of the anal canal and reported 3 cases which were verified histologically. In 1930 Angevine [11] studied at autopsy a case showing 3 distinct malignant rectal tumors, 1 of which was an acanthoma. Rosser,[12] in studying the relationship of chronic inflammatory lesions of the rectum to neoplasia, described 3 microscopically proved epidermoid carcinomas of the anus. Gabriel,[13] in a study of the end-results in the treatment of 370 cancers of the rectum, recorded 12 cases of squamous cell carcinoma of the anus and anal canal. Of these, 8 were assessed as "operable" and 4 as "inoperable." Recently Lockhart-Mummery [14] reported the treatment of an epithelioma of the anus occurring in a man 56 years of age. A combination of radon seeds and radium needles inserted beneath and around the tumor was used. There was no evidence of recurrence at the time of reporting, nearly one year after treatment.

REPORT OF CASES

CASE 1.—*History.*—Mr. Y. V., a Mexican laborer, aged 35, presented himself in the outpatient department in June, 1926, complaining of severe constipation and a stinging pain in the anorectal region during defecation followed by a slight amount of bleeding. A diagnosis of condyloma of the anus and cryptitis was made and appropriate therapy was advised. He refused treatment, and was not seen again for two years. On his return, in 1928, he complained of "piles" which had caused considerable pain, difficulty in expelling the feces and occasionally bright

6. Lockhart-Mummery, J. P.: Diseases of the Rectum and Colon, New York, William Wood & Company, 1923.

7. Mecray, P. M.: Epithelioma of the Anus in a Case of Imperforate Anus, S. Clin. North America **6**:1623 (Dec.) 1926.

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9. Hawe, P.: Carcinoma, a Complication of Piles, Brit. M. J. **2**:349 (Aug. 27) 1927.

10. Plisson, M. L.: Epithélioma ano-rectal, Progrès méd. **42**:1408 (Sept. 10) 1927.

11. Angevine, D. M.: Three Primary Malignant Epithelial Tumors of the Ano-Rectal Region Occurring in One Person, Canad. M. A. J. **23**:38 (July) 1930.

12. Rosser, Curtice: Etiology of Cancer of the Anus, Am. J. Surg. **11**:328 (Feb.) 1931.

13. Gabriel, W. B.: End Results of Perineal Excision and Radium in the Treatment of Cancer of the Rectum, Brit. J. Surg. **20**:234 (Oct.) 1932.

14. Lockhart-Mummery, J. P.: Epithelioma of Anus Treated by Radium, Proc. Roy. Soc. Med. **26**:589 (March) 1933.

red blood in the stool. During the previous three weeks he had suffered severe pain in the right side of the chest, associated with coughing.

Physical Examination.—Examination revealed an emaciated man of 37, apparently in distress. The right side of the chest showed the classic findings of a massive pleural effusion. There was exquisite tenderness to deep palpation in the right side of the hypochondrium, without other abdominal findings. A girdle ulcer with a firm base occupied the lower half of the anal canal, at the base of which was a "sentinel" pile. An ulcerative proctitis extended above this ulcer for 2½ inches (6.4 cm.). A blood test showed 17,600 white cells, with 79 per cent polymorphonuclears. The sputum was negative for the tubercle bacillus. The Wassermann reaction of the blood was 4 plus.

Course.—The course was progressively downward, with a septic temperature and an increase in the severity of the symptoms in the chest. Death occurred after two months.

Autopsy.—The essential pathologic findings exclusive of the acanthoma were limited to an extensive amebic colitis and an abscess of the liver with diaphragmatic extension resulting in empyema on the right side. The anus was deeply fissured, with a large necrotic ulcer. No local extension or regional adenopathy was found. The microscopic sections of the anal ulcer showed a squamous cell carcinoma graded 1 as described by Broder.

CASE 2.—*History.*—Mrs. P. R., aged 40, was admitted to the Los Angeles County General Hospital with a complaint of malaise, weakness, loss of appetite, severe constipation and difficulty in expelling the feces. She first noticed these symptoms three months before admission. One month after the onset she was troubled with flatulence which had been progressively worse until the date of admission. The constipation virtually amounted to obstipation during the immediately preceding month. Twice during the course of the disease she had noticed bleeding from the rectum which she ascribed to hemorrhoids.

Physical Examination.—Examination revealed a well nourished Mexican woman not in acute distress. The physical findings were essentially normal except for the local pathologic process. The posterior wall of the vagina was pushed forward by a hard mass, giving the impression that the rectum was packed with feces. Digital examination of the rectum revealed a coarsely nodular, friable, ulcerated mass originating at the anorectal junction and extending upward into the pelvis beyond the length of the examining finger. The lesion occupied the entire circumference of the rectum except for a strip along the anterior wall which measured 1 cm. in width. Proctoscopic examination showed the lesion to extend for approximately 5 cm. above the anorectal junction. The perirectal tissue was moderately indurated. Laboratory examination, including the injection of a radiopaque enema, gave negative results except for a Wassermann reaction of 1 plus and a Kahn reaction of 2 plus.

Course.—A single loop colostomy was made, and the distal loop transplanted to the pelvic retroperitoneal space. The postoperative course was hectic, and on the nineteenth day a perineal incision was made into a large perirectal abscess. Ten days later the lower loop of the colostomy was resected, the abdominal approach being used. The postoperative course was stormy. Death occurred in four days with clinical evidence of acute generalized peritonitis.

Autopsy.—The significant organic changes were limited to the neoplasm and the changes incidental to the surgical assault directed toward its destruction. The rectum and the anal canal remained in the pelvis. The mucosa of the portion of

bowel immediately proximal to the tumor was superficially ulcerated, but showed no other essential disease. At the anorectal junction was a firm mass, the lower margin of which was polypoid, ragged, necrotic, foul smelling and ulcerated. The neoplastic tissue above the ulcer produced a considerable degree of stenosis. The perirectal tissue was indurated and in the region of the posterior vaginal wall showed the remains of an abscess which was draining into the vagina. A careful search of the pelvic lymphatics and the inguinal nodes showed no metastatic deposits, either in the gross specimen or by microscopic section. The abdominal cavity showed the typical changes of acute generalized peritonitis.

Histologic examination of the growth revealed a typical malignant growth of epithelial cells of the squamous variety. Numerous pearl bodies were present. The carcinomatous cells were found invading the muscularis of the bowel, but

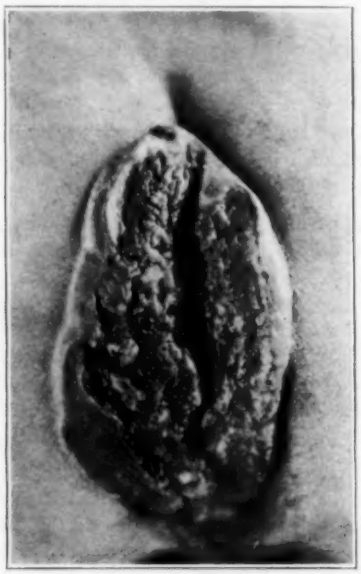

Fig. 1 (case 3).—Exophytic type of acanthoma of the anus.

none was found in the perirectal fat. An extensive infiltration of polymorphonuclear wandering cells was present throughout the tumor. Microscopically the tumor was graded according to Broder's classification as grade 1.

CASE 3.—*History.*—Mr. J. H., aged 60, was admitted to the Los Angeles County General Hospital, complaining of constipation for many years, a progressively enlarging ulcerating growth at the anus and pain in the region of the tumor when sitting. The growth appeared nine months previously as a "bluish pimple" in the perianal skin. The tumor was firm and painless, and during the early portion of its growth invaded the anal mucosa. During the immediately preceding three months the growth became painful to pressure and bled when traumatized. The patient's history was irrelevant except for a syphilitic infection thirty years before admission which had been vigorously treated.

Physical Examination.—Examination revealed a well preserved and well nourished white man who did not appear to be acutely ill. The essential physical find-

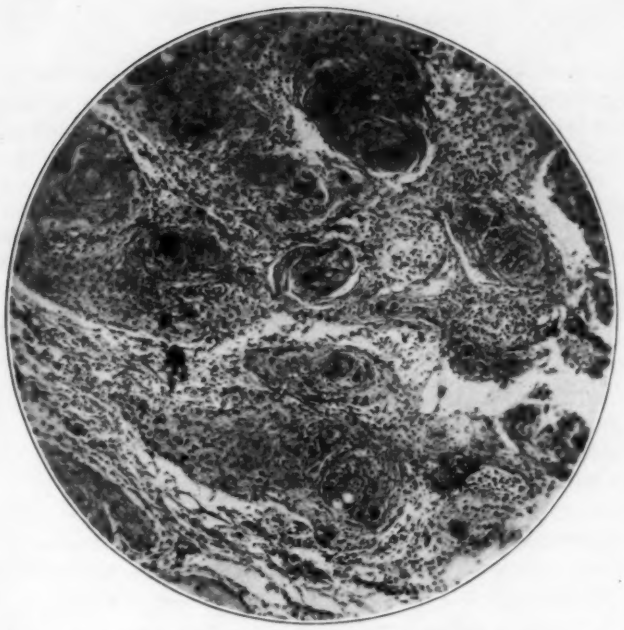

Fig. 2 (case 3).—Photomicrograph of well differentiated tissue with numerous pearl bodies; hematoxylin and eosin stain; × 165.

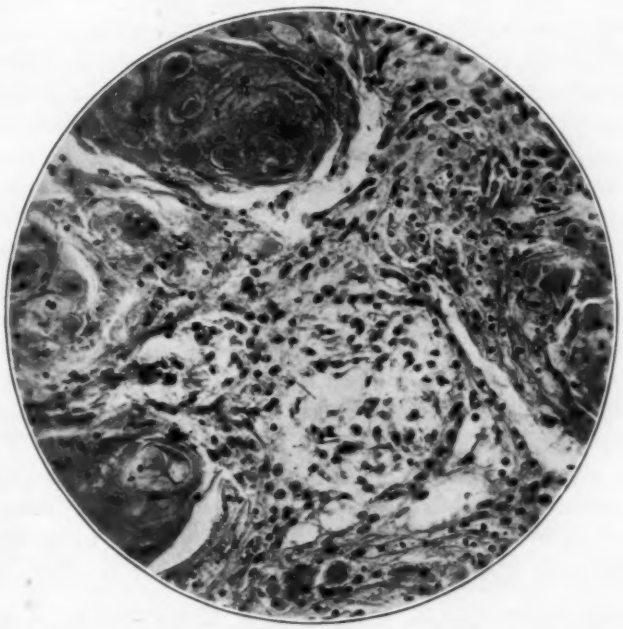

Fig. 3 (case 3).—Photomicrograph of squamous cell epithelium. An occasional mitotic figure is seen; hematoxylin and eosin stain; × 300.

ings were limited to the anal growth. The anal orifice was obscured by an elliptic, velvety, papillomatous, ulcerated and necrotic tumor 12 by 8 cm. in diameter which occupied the perineum from the central tendinous point posteriorly to a point 1 cm. anterior to the tip of the coccyx. The lateral margins were approximately 1 cm. medial to the tuber ischii. The central portion was deeply fissured and ulcerated, and discharged a seropurulent fluid. The margins were dusky, smooth, rolled and sharply limited. The tumor was hard except in the midportion, where necrosis had taken place. The tumor caused considerable constriction of the anal orifice, and extended upward to the lower surface of the levator ani. No enlarged lymph nodes were found in the pelvis or in the inguinal region. The laboratory findings were negative except for a Wassermann and Kahn reaction of the blood serum of 4 plus.

Course.—The entire growth and the fat in the ischiorectal fossa were resected with the Percy cautery following removal of a specimen for biopsy. The patient failed to respond postoperatively, and the condition became toxic. He died of circulatory failure on the sixth day following the operation.

Autopsy.—A complete examination of the body revealed no remaining carcinoma. Otherwise the essential changes were a marked generalized arteriosclerosis with coronary sclerosis. Histologic examination of the specimen removed at operation showed a grade 1 (Broder) squamous cell carcinoma.

COMMENT

Acanthomas of the anus usually arise at the mucocutaneous junction. The lesion is sharply demarcated and becomes ulcerated late in its course. The growths may be of the exophytic, exuberant type (case 3) or the endophytic type which occupies the anal canal without producing an externally visible tumor, as illustrated by cases 1 and 2. Clinically the tumor produces a period of constipation of varying length before localizing symptoms appear. Later, the patients complain of a sense of fulness in the rectum, difficulty in expelling the feces and a minor amount of bleeding, and in the exophytic type the tumor is often described. The endophytic type is frequently associated with hemorrhoids. Early ulceration associated with excruciating pain, as emphasized by Rankin, Bargen and Buie,[15] was not prominent in our cases.

Several views have been expressed regarding the etiology of this neoplasm. The exciting cause is veiled in the obscurity enclosing the etiology of malignant growths elsewhere in the body. Pack [2] supports the Cohnheim theory of "cell rest" and relates its probability to the complex embryologic development of this particular region. The theory ascribing the development of cancer to the changes resulting from chronic irritation has been especially emphasized in this location owing to the nature of the secretions present, the inability to maintain strict cleanliness, and, associated with these factors, the occurrence of such

15. Rankin, F. W.; Bargen, J. A., and Buie, L. A.: The Colon, Rectum and Anus, Philadelphia, W. B. Saunders Company, 1932.

lesions as fissures, fistulas and hemorrhoids. Opposed in part to that theory is the case described by Mecray [7] of an epidermoid carcinoma occurring at the site of an imperforate nonfunctioning anus. It must be conceded, however, that in this case the element of chronic irritation is not completely excluded. The ulcerative colitis due to Endameba histolytica in case 2 is an added factor of chronic irritation. Brofeldt [3] maintained that leukoplakia is frequently present in the anal canal and has a relation to anal cancer similar to that which its homolog in the oral cavity has to the development of buccal carcinoma. In the 3 cases reported here it seems noteworthy that a positive Wassermann reaction of the blood serum occurred in each case, although the reaction present in case 2 was only 1 plus with an accompanying Kahn reaction of 2 plus. The reactions were repeated in each case. These cases were not seen sufficiently early to determine whether this factor operated through the development of leukoplakia. The one patient seen two years before the tumor was diagnosed was thought to have an anal condyloma. In the case reported by Wallon [8] a diagnosis of "mucous patches" was made three years before the acanthoma developed, and the patient was given appropriate antisyphilitic treatment. It appears that the syphilitic infection furnished a favorable soil on which the epithelioma developed. In cases 1 and 2 of this report an associated rectal lesion produced chronic irritation complicating the problem of determining the underlying cause.

From the point of view of pathology these growths are of a comparatively low degree of malignancy. Each of the three cases we studied was classified as grade 1 (Broder). The tumor is at times found penetrating the muscular coats of the bowel, suggesting the possibility of direct extension into the ischiorectal fossae. None of the cases described showed metastases to the regional nodes. Waring [16] discussed the mode of metastases to the inguinal nodes via a lateral and a medial channel. No secondary deposits were found in this group of nodes although a careful search for them was made.

The therapeutic deductions from these data are obvious. The lesion could be cured in its early stages by local removal, preferably by the cautery, as suggested by Charles Mayo.[17] Later in the course of the disease the anus, anal canal and lower portion of the rectum should be radically resected and an extensive dissection of the inguinal nodes accomplished. For epitheliomas graded 3 and 4 (Broder) Rankin,

16. Waring, H. J.: Surgical Treatment of Malignant Disease, New York, Oxford University Press, 1928, p. 127.

17. Mayo, Charles: The Choice of Operative Procedure in Cancer of the Rectum and Pelvic Colon, Collected Papers of the Mayo Clinic, Philadelphia, W. B. Saunders Company, 1916, vol. 8, p. 322.

Bargen and Buie [15] advocated treatment by irradiation in perference to surgical intervention. Wallon,[8] Lockhart-Mummery [18] and Gabriel [13] have reported success in curing this lesion by irradiation, although the degree of differentiation of the tumor as shown by its histopathology does not particularly suggest that it is radiosensitive.

SUMMARY

1. Forty acanthomas of the anus reported in the literature of the past two decades are reviewed.

2. The clinical course and findings at autopsy in 3 cases of acanthoma of the anus in a series of 46 malignant tumors of the anorectal region are recorded.

3. Each of the 3 patients presented an associated syphilitic infection, evidenced by positive Wassermann and Kahn reactions of the blood serum.

4. These tumors are of a comparatively low grade of malignancy. Each of the 3 tumors reported here was classified grade 1 (Broder).

18. Lockhart-Mummery (footnotes 6 and 14).

A NEW INSTRUMENT FOR INTRAVESICAL IRRADIATION

OSWALD S. LOWSLEY, M.D.
AND
STANLEY L. WANG, M.D.
NEW YORK

Therapy with ultraviolet rays from a quartz mercury vapor arc lamp has for a long time been an important part of treatment of postoperative and inoperable genito-urinary tuberculosis. The older type of air-cooled quartz mercury vapor arc lamp, also the newer more powerful variety, and the water-cooled quartz mercury vapor arc lamp have been utilized. The air-cooled lamp is almost a specific in the healing of sinuses following nephrectomy and epididymectomy for tuberculosis. Similar exposures over the regions of the bladder and kidneys at regular intervals over long periods are given as a routine in the treatment of urinary tuberculosis. Since therapy of this kind has been useful externally it is reasonable to think that it might have a good effect in the bladder if it could be suitably applied. However, we have not been able to employ it satisfactorily until recently.

Caulk and Ewerhardt [1] reported treatment by direct internal ultraviolet irradiation of the bladder of a patient from whom a tuberculous kidney had been removed several years previously and who still had persistent ulceration in the bladder. Using a cold quartz orificial applicator, insulated to protect the urethra, they arranged a device to introduce both air and ultraviolet irradiation into the interior of the bladder. They stated that as far as they could determine it was the first time that such a technic had been attempted.

A few months later we obtained a quartz mercury vapor arc lamp of the vacuum discharge type, with a bladder applicator, constructed according to our specifications.[2] The applicator is made of a new material produced for physical, photochemical, physiologic and thera-

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From the Department of Urology (James Buchanan Brady Foundation), New York Hospital.

Read before the Section on Genito-Urinary Diseases of the New York Academy of Medicine.

1. Caulk, John R., and Ewerhardt, F. H.: Direct Internal Irradiation of Ultraviolet to the Bladder, Arch. Phys. Therapy **13**:325 (June) 1932.

2. Mr. Frederic W. Robinson of the Hanovia Chemical Company cooperated in the manufacture of this instrument.

peutic experimental work and also for study of the "Raman effect." The tube is made of clear fused quartz to transmit the rays readily and operates at a little above room temperature. It is said to be practically monochromatic, and approximately 85 per cent of the generated light

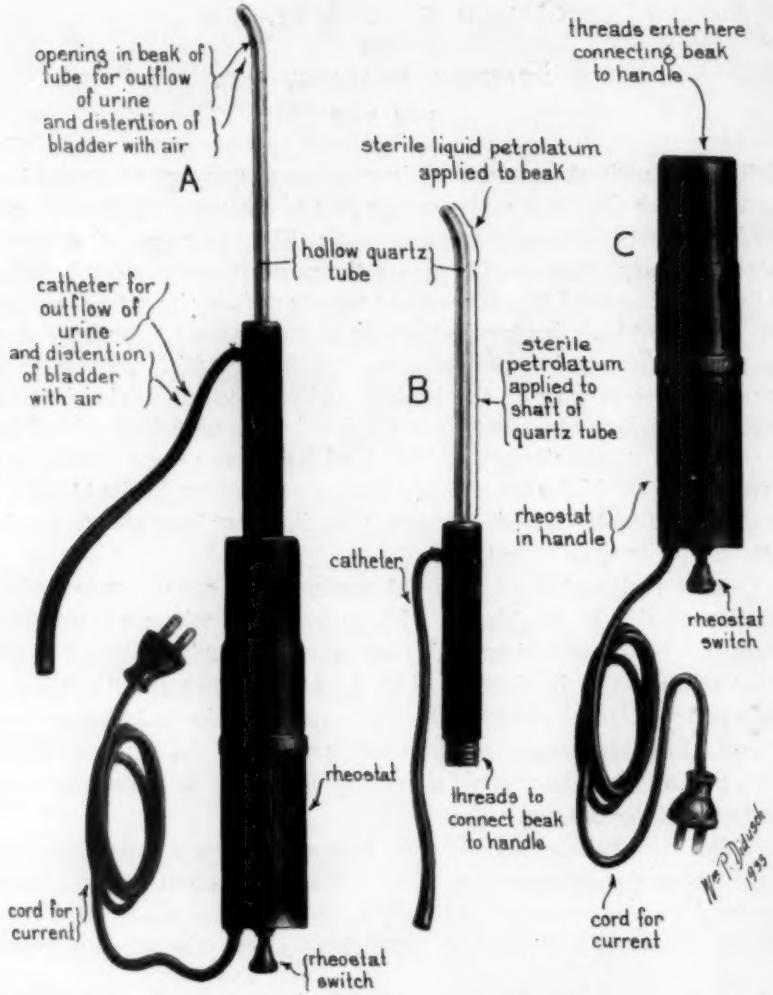
opening in beak of tube for outflow of urine and distention of bladder with air
A
catheter for outflow of urine and distention of bladder with air
rheostat
cord for current
rheostat switch
hollow quartz tube
sterile liquid petrolatum applied to beak
B
sterile petrolatum applied to shaft of quartz tube
catheter
threads to connect beak to handle
threads enter here connecting beak to handle
C
rheostat in handle
rheostat switch
cord for current

Fig. 1.—*A* shows the assembled instrument, consisting of rheostat, cord, catheter for the overflow of urine and distention of the bladder with air and the hollow quartz tube for the passage of the irradiation current. *B* and *C* show the instrument disassembled.

is in the band of 2,537 angstroms. The applicator is about the same length and shape as a Brown-Buerger cystoscope, measuring about 24 French in diameter. There is an extra tube built into the quartz

with a circular opening or eye at the distal end and with a rubber tube attached to the other extremity. The tube is for the purpose of catheterizing the bladder. After the bladder is emptied air is insufflated through the tube to distend the organ slightly before irradiation. Following the treatment an instillation can be made through the tube if desired. The applicator, except at the distal end, is smeared with sterile petrolatum to prevent the irradiation of the urethra, and sterile liquid petrolatum, which permits the passage of the rays, is used on the part that enters the bladder. The instrument offers a simple and practical

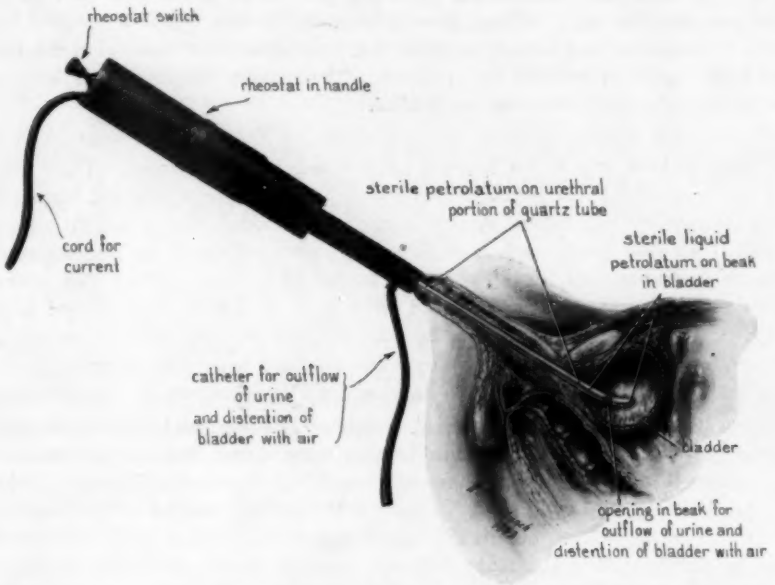
rheostat switch
rheostat in handle
sterile petrolatum on urethral portion of quartz tube
sterile liquid petrolatum on beak in bladder
cord for current
catheter for outflow of urine and distention of bladder with air
bladder
opening in beak for outflow of urine and distention of bladder with air

Fig. 2.—A sagittal section of the bladder and urethra with the instrument in place and the bladder distended with air for the dissemination of irradiation in the diseased bladder.

means of irradiation of the interior of the bladder. The bladder can be emptied, then distended with air without pressure and irradiated at one operation and with little discomfort to the patient. The applicator passes through the urethra easily and can be used equally well in either male or female patient. Exposures up to thirty seconds have thus far been used, depending on the reactions elicited. The reactions are of a transitory character, lasting for a few hours.

Eleven patients are receiving internal treatments. In four the condition seems to be definitely improved, in four others slightly improved, and in three there is no improvement. Several have badly damaged

bladders owing to extensive involvement, which offers a severe test for any form of therapy. To show the kind of patients treated the series is briefly described.

CASE 1.—A woman, aged 22, married, weighing 74.1 Kg., had tuberculosis of the right ankle in childhood which healed after a year. About two and a half years ago, following childbirth, she began to have urinary frequency, hematuria, pain in the bladder and burning on urination. A right nephrectomy for tuberculosis was done on Aug. 12, 1931. The wound healed in two weeks. The urinary frequency has persisted day and night with pain in the bladder. The urine still contains acid-fast bacilli in catheterized specimens. The capacity of the bladder is 30 cc., the walls are trabeculated, there are ulcerations at the neck and on the right side, and the right ureteral opening is atrophied (the left is apparently normal). The patient has been treated for five months with intravesical irradiation, and there has been marked improvement. The urinary frequency has lessened, and the pain in the bladder has diminished.

CASE 2.—A woman, aged 25, married, weighing 47.8 Kg., had tuberculosis of the lungs in 1924, which was arrested after a year in a sanatorium. Three years ago urinary burning and frequency developed. A diagnosis of bilateral inoperable renal tuberculosis was made. A year later the left kidney suppurated, the general condition became grave, and a nephrectomy was performed as an emergency measure to prolong her life. The wound healed after nine months. The urinary frequency was lessened, but continued, with pain in the bladder. Urine taken from the bladder reveals acid-fast bacilli. She has received irradiations to the bladder for about five months, although she has been somewhat irregular in her attendance at the clinic. There has been a slight improvement in the symptoms.

CASE 3.—A man, aged 30, married, weighing 70.8 Kg., had pain in the right lumbar region in April, 1929, which became more severe and was accompanied by a high fever. A right nephrectomy for tuberculosis was done at another hospital in April, 1929. He felt well until May, 1932, when a sinus developed in the scar of the nephrectomy which still drains rather profusely. A few months later he noted urinary frequency and was referred to our clinic for treatment. The interior of the bladder shows a little roughening of the mucosa at the fundus and slight injection of the trigon. There are acid-fast bacilli in the urine. He has a pulmonary lesion which is apparently inactive. Because of the unusual history of the sinus and its atypical character, roentgenograms were made of the spine in the lumbar region which revealed spinal caries. It is believed that the sinus is due to the caries, and the patient is now receiving orthopedic care. The bladder has been irradiated for three months and the urinary symptoms are slightly lessened.

CASE 4.—A woman, aged 28, married, weighing 51.9 Kg., became pregnant in 1922; at the fourth month general edema developed. Her physician diagnosed the condition as a "pus kidney," and a therapeutic abortion was done. Shortly afterward urinary frequency occurred, which gradually increased in severity. A right nephrectomy for tuberculosis was done in May, 1930. Since then the patient has had slight urinary frequency and pain on urination. The disease seems to be of a relapsing type, as there are periods of almost complete relief which are broken by a recurrence of marked symptoms. The urine contains a large amount of pus and acid-fast bacilli. There is a mild thyroid disturbance at times. She

has received irradiation for three months, and the condition is improved; however, the remittent nature of the disease presents difficulties in determining the condition.

CASE 5.—A woman, aged 22, unmarried, weighing 48.7 Kg., had tuberculous peritonitis in 1924, and after several years of hygienic care had no further symptoms. Since 1930 she has had pain in the region of the kidneys, mostly on the right side, with urinary frequency and burning. The condition was diagnosed as inoperable bilateral renal tuberculosis. The capacity of the bladder is 130 cc., and the interior is essentially normal except for reddening around the left ureteral opening, below which there is a red bleb. The bladder has been irradiated for four months, and while there has been occasional temporary lessening of pain after the treatments, the condition has not improved.

CASE 6.—A woman, aged 24, unmarried, weighing 50.2 Kg., had tuberculosis of the lungs in 1928, which apparently became arrested after seven months in a sanatorium. There has been an extensive pustular acne for the last two years. Pus in the urine was discovered four years ago. Urinary frequency, both day and night, and pain in the back developed a few months after finding pus in the urine. The patient lost weight and strength. A right nephrectomy for tuberculosis was performed at another hospital on June 6, 1932. She was subsequently referred to our clinic suffering with urinary frequency, pain in the bladder and occasional hematuria. She has received internal irradiation for two months, and the condition has improved.

CASE 7.—A woman, aged 25, unmarried, weighing 42.5 Kg., began to have urinary frequency in 1928. It became more severe, and the right kidney was removed for tuberculosis on Nov. 14, 1930. The frequency continued and an ulceration in the bladder underwent fulguration several times without lasting results. Tuberculosis of the lungs developed in 1931, which became quiescent after a year of rest, diet and fresh air. The urinary symptoms persisted. The bladder is extensively diseased; the capacity is 30 cc., and there are numerous trabeculations and disseminated ulcerations, particularly in the regions of the ureteral openings. Internal irradiation has been given for four months, with definite symptomatic improvement.

CASE 8.—A woman, aged 40, married, weighing 66.8 Kg., has had pain in the bladder before urination, great urinary frequency and pain in the kidneys and along the urethra since 1924. She has been treated by numerous physicians and at several hospitals without relief. Endoscopy showed ulcerations of an odd villous appearance along the urethra. Cystoscopy showed the same productive form of ulcerations within the bladder, widely distributed and somewhat ecchymotic. The capacity of the bladder is about 30 cc. The lesions are not definitely characteristic of tuberculosis. Many remedies and various therapeutic procedures have been tried without affording relief. Internal irradiation for five months has not given periods of lasting relief. Recently longer irradiation, up to thirty-five seconds, of both urethra and bladder, followed by an instillation of 1 ounce (28.34 Gm.) of 2 per cent of a preparation similar to oil of cajuput in olive oil, have afforded symptomatic relief for from twenty-four to thirty-six hours after treatment.

CASE 9.—A woman, aged 31, married, weighing 59.8 Kg., at the age of 13 had pleurisy with effusion; aspiration was performed and a large amount of fluid removed. Recovery occurred after a long period. During June, 1931, pain occurred in the bladder and right kidney, accompanied by slight urinary frequency and burning. She was treated for five months in a sanatorium for tuberculosis, where

it was determined that there was no pulmonary involvement. A right nephrectomy for tuberculosis was performed on June 15, 1932, at another hospital, and the wound healed in fifteen days. The urinary frequency and pain in the bladder continued, and she was referred to our clinic. The capacity of the bladder is 110 cc.; the left ureteral opening is enlarged, the right ureteral opening is not visible and there is an irregularly shaped ulcer of dull appearance above the region of the right ureteral opening. The patient has received internal irradiation for about five months and there is a little improvement.

CASE 10.—A woman, aged 32, unmarried, weighing 61.1 Kg., had hematuria in February, 1924, followed by urinary frequency and pain in the bladder. A right nephrectomy for tuberculosis was performed on Nov. 21, 1924, at another hospital. After two years of treatment with rest the symptoms disappeared. Urinary frequency recurred in 1930, and later she was referred to our clinic. The capacity of the bladder is 75 cc., the right ureteral opening is not visible, the left is distended and distorted and there is extensive trabeculation with widespread ulcerated hemorrhagic areas. The urine is turbid, and there is macroscopic evidence of blood and considerable pus. Internal irradiation for five months has made little if any change, except a temporary lessening of the symptoms.

CASE 11.—A woman, aged 47, married, weighing 81.6 Kg., at the age of 9 had a disease of the bone in the left forearm, apparently tuberculous, which healed after a year. In 1925 urinary frequency developed, with pain in the bladder and general debility. A right nephrectomy for tuberculosis was performed a year later, and the wound healed in a short time. The urinary frequency continued for two or three years, then subsided; fulguration was used twice for the ulcerations in the bladder. Since then the only symptoms have been occasional pain in the bladder and a slight intermittent urinary frequency. The capacity of the bladder is 230 cc., and the wall is essentially normal except for a little redness around the left ureteral opening. She has received internal irradiation for six weeks, and there has been some improvement.

COMMENT

It is apparent that no attempt was made to select the patients to receive the irradiation, as many have lesions in the bladder which are very extensive and function is probably partially crippled. No conclusions can be drawn from so small a series, but it would seem that postoperative treatment of this kind is indicated after a nephrectomy in patients with small lesions in the bladder that are not of long standing. Fresh air and therapy with a quartz mercury vapor arc lamp hasten the healing of external lesions, and there is reason to believe that similar results should follow the same treatment of internal lesions. Even in widespread involvement of the bladder several patients have thought that there was lessening of sensitivity in the bladder. This form of therapy seems better tolerated than any other local treatment that we have tried. The applicator was planned with the thought that there must be as little local disturbance as possible, and it seems successful in that respect. Patients who have received external therapy with a quartz mercury vapor arc lamp are usually willing to try the treatment internally.

It has been suggested that irradiation might have some field of usefulness in urology other than in the treatment of urologic tuberculosis. Eighty-five per cent of the generated light is said to be in the band of 2,537 angstroms, which is considered bactericidal. A patient with chronic posterior gonorrheal urethritis is now being treated and it is hoped to treat a sufficient number with a similar infection on which to base worth-while conclusions.

Caulk and Ewerhardt noted the disappearance of an infection by colon bacilli in their patient after four periods of irradiations. Other observers have reported that the use of a quartz mercury vapor arc lamp is effective against colon bacilli. We have not yet begun treatment of patients with such an infection.

CONCLUSIONS

1. The instrument we have used seems to be satisfactory for emptying the bladder, introducing air and irradiating the wall of the bladder. In the series of patients treated the results have been encouraging and warrant further trial of the procedure.

2. This instrument may also be utilized to treat sinus tracts caused by tuberculosis in any part of the body.

899 Park Avenue.

126 East Sixty-First Street.

TRAUMATIC VASOSPASM

A STUDY OF FOUR CASES OF VASOSPASM IN THE UPPER EXTREMITY

EDWIN P. LEHMAN, M.D.
UNIVERSITY, VA.

Disturbances of the sympathetic impulse in the extremities are still too little understood. From time to time reports of conditions suggesting dysfunction of the sympathetic system affecting the blood supply reach the literature. The clinical expressions of sympathetic dysfunction in any group of cases are apt to be variable and difficult to correlate. Among the array of conditions in which hyperactivity of the sympathetic system can be descried, traumatic vasospasm may be picked out as a more or less definite entity. Individual instances of traumatic vasospasm are so different from each other in their details that the total clinical picture is not easy to visualize. They have two factors in common: (1) trauma, usually received at some time considerably earlier than the patient is seen, and (2) evidence of vasospasm. Confusion arises because one often sees additional disturbances of somatic sensory and motor function as well as so-called trophic changes. These disturbances are sometimes bizarre in that they bear no anatomic relationship to the injury or to the area affected by arterial spasm. Some patients present an extraordinary variety and intensity of disturbances; in others none may be present. Their relationship to or identity with hysteria is usually debatable. The reaction to treatment in individual cases is correspondingly irregular. Until a much larger number of these curious conditions are recorded in detail knowledge of them will remain defective. For that reason I am reporting four cases of sympathetic disturbance following injury, all of which can probably be classed as traumatic vasospasm. Attention may be called to a contribution by Morton and Scott[1] in which these and related conditions are discussed in full.

REPORT OF CASES

CASE 1.—*Superficial Wound of Palm.—Infection.—Vasospasm of five months duration. Unanatomic sensory disturbance. Loss of forearm motor power with spastic state of muscles. Rapid complete recovery following fever.*

W. A. M., a white man, aged 28, a laborer, entered the hospital on Aug. 20, 1930, two weeks after a superficial laceration in the palm of the right hand. At

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From the Department of Surgery and Gynecology, University of Virginia School of Medicine.

Abridged from a paper read before the Ohio County Medical Society, Wheeling, W. Va., April 14, 1933.

1. Morton, J. J., and Scott, W. J. M.: Some Angiospastic Syndromes in the Extremities, Ann. Surg. **94**:839 (Nov.) 1931.

first he continued to work. Three days later the hand became swollen and painful, but he still worked for three more days, and then went to bed and applied poultices for about a week. The wound in the palm was then opened by his local physician. The operation was followed by an evidence of spreading infection, including lymphangitis, and he was referred to the hospital. Under nitrous oxide anesthesia the midpalmar space was drained with prompt and apparently complete recovery. He was discharged four days later.

The wound drained for a period and then healed. When attempting to use the hand, the patient found much weakness in the fourth and fifth fingers with diminution in sensation in this area. The scar was painful. He noticed "poor circulation" in the right arm which felt "heavy and dull." He also noticed that it was cooler than the other hand. There was no pain except on movement. Exposure to cold caused numbness of the inner half of the hand. He was readmitted to the hospital

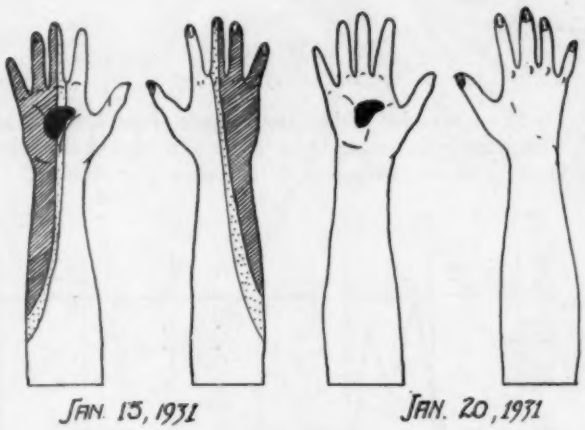

Fig. 1 (case 1).—Chart of sensory changes in the right hand. Note the relation of the wound at the center of the area of hyperalgesia to the sensory loss. Note also the fact that the sensory loss does not correspond to the distribution of the peripheral nerves. Complete return of sensation is indicated four days after a short period of fever. The shaded areas indicate marked hypesthesia and hypalgesia; the stippled areas indicate moderate hypesthesia and hypalgesia; the black areas indicate hyperalgesia.

on Jan. 13, 1931, with the diagnosis of a vasospastic state following trauma and infection.

A general examination made at this time revealed no abnormalities. Local examination showed markedly decreased power in the right hand, especially in the third and fourth fingers, with a healed scar in the palm of the hand. The patient held the third, fourth and fifth fingers in semiflexion. Sensory changes, which were unanatomic, are shown in figure 1. The hand was bluish, cold and moist. There was some atrophy of the subcutaneous tissues and skin. The flexor muscles of the forearm were in moderate spasm, particularly on the ulnar side, suggesting the "reflex spasm" of Weir Mitchell.

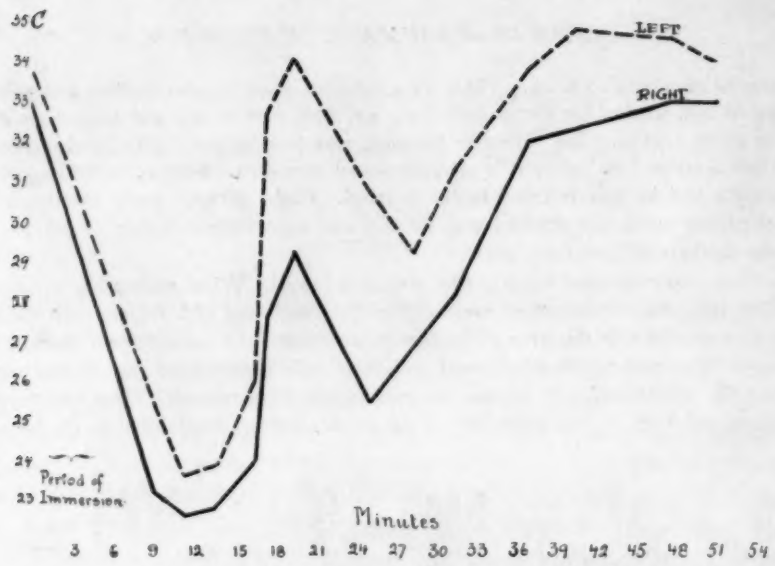

Fig. 2 (case 1).—Curve for surface temperature of the hands following immersion for three minutes in water at O C. There is a marked delay of the diseased hand in reaching the control temperature. Compare with figure 4.

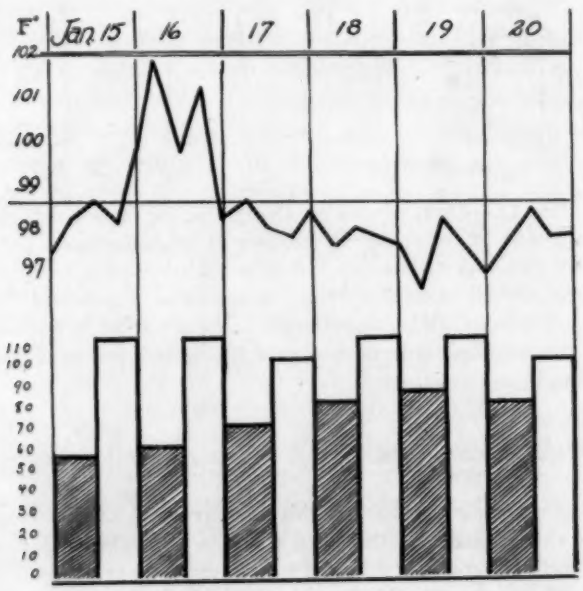

Fig. 3 (case 1).—This chart illustrates the progressive increase in strength of the diseased hand during six successive days. On January 15 typhoid vaccine was given, and on January 16 the patient had an infection of the upper respiratory tract with fever. From that date on strength increased from 55 to 80 per cent of normal. The upper graph shows the oral temperature; the shaded areas indicate the ergometer readings on the diseased hand; the white areas, the readings on the normal hand.

On Jan. 15, 1931, the surface temperature reactions to immersion in ice-water for three minutes were studied (fig. 2). There was a slower return of the surface temperature to the usual level in the involved as compared to the opposite hand. The exposure to cold water caused extreme pain. The hand returned to its previous level of surface temperature in about one hour.

Fifteen minutes later mixed typhoid vaccine, 25,000,000 organisms, was given intravenously. There was no effect on the body temperature. One hour and thirty minutes after the injection the grip in the right hand suddenly became approximately normal in strength; movements became free, and the hand became flushed. This curious reaction disappeared in fifteen minutes, and the hand returned to its previous condition.

The following day an acute cold with a rise in temperature to a maximum of 101.8 F. developed. The fever lasted twenty-four hours (fig. 3). From the onset

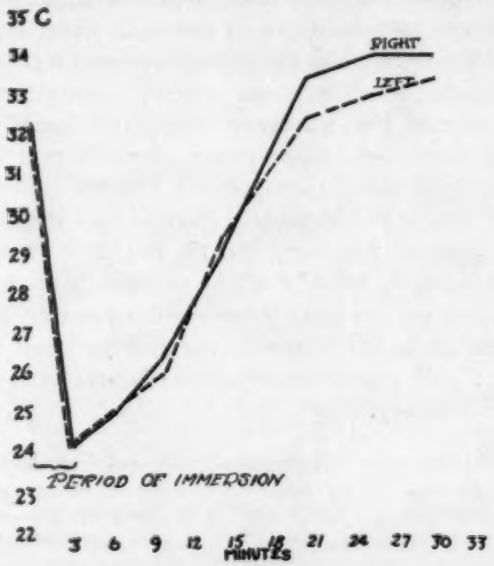

Fig. 4 (case 1).—Response of the two hands to immersion in ice-water four days after the fever. Compare with figure 2. The curves are now almost identical. On this date (Jan. 20, 1931), sensory changes had disappeared, and strength had risen from 55 to 80 per cent of normal.

of this fever the patient's hand began to improve. The grip increased; the color became pink, and the neurologic changes disappeared.

An ordinary grip ergometer was first used on the day of the injection of typhoid vaccine. A progressive increase of strength in the hand is shown, as illustrated by the diagram superimposed on the temperature curve (fig. 3). The residual defect of 20 points, shown four days later, may perhaps be ascribed to the atrophy of disuse.

Four days after the onset of the fever the surface temperature of the two hands was equal, and the test with ice-water showed equally prompt reactions (fig. 4). On this occasion no pain was caused by exposure to cold. A third test

six days after the second showed a similar curve. A sensory examination four days after the fever showed the hand to be normal, except for a slight hyperesthesia around the scar (fig. 1).

The patient was discharged from the hospital two weeks after admission with an apparently normal hand except for a slight weakness of the grip. On March 6, 1933, over two years following treatment, he wrote: "My hand is all right except the little finger. In cold weather it bothers me some."

The patient was seen in June, 1933. An examination showed equal and excellent power in the two hands and no differences in color, moisture or surface temperature. The little finger tends to become numb on cold mornings. The patient is capable of continuous hard manual labor and has been so since his discharge from the hospital.

This patient had a loss of motor function, unanatomic hypesthesia, coolness, blueness and moistness of the right hand, lasting nearly five months. The vasospasm was temporarily released following an injection of typhoid vaccine which gave no primary constitutional reaction and permanently released after a fever of twenty-four hours' duration. With the release of vasospasm, motor power promptly returned and clearcut unanatomic sensory changes disappeared. At the outset the neurologist who saw this patient in consultation inclined to a diagnosis of hysteria. It is hardly probable, however, that the objective records of response of surface temperature to cold could be so logically produced by hysteria. Further comment on this point is made subsequently. It must be noted in passing that an earlier diagnosis would have saved this man nearly five months of pain and uselessness and his insurance company a considerable sum of money.

CASE 2.—*Injury to palm with tendon division and immediate suture. Unsatisfactory tendon healing. Slight vasospasm. Loss of motor power in adductors of thumb. Spastic state of flexor muscles of forearm. Unanatomic hypesthesia of finger. Artificial fever induced. Strength of thumb adductors nearly tripled. Flexor spasm released. Reaction to cold improved. Patient still under treatment.*

W. E. T., a right-handed white farmer, aged 46, was first seen in the outpatient department on Jan. 3, 1933, with an incised wound of the distal portion of the palm of the left hand, severing the flexor tendons to the middle finger. The interphalangeal joints of the first finger were ankylosed from an old injury. A longitudinal incision was made over the course of the tendons which were sutured. The wounds healed cleanly. When last seen in the outpatient department on Jan. 28, 1933, it was noted that there was practically no motion in the middle finger.

I first saw the patient on March 8, 1933. At the time he was complaining of almost complete disability of the left hand, without pain. An examination showed the scar of the operation and the scar of the original injury (fig. 5). The hand was slightly blue, cool and moist as compared to the right hand. There was no difference in the radial pulses. Extension at the metacarpophalangeal joints of the hand was limited by about 15 degrees. Flexion at this joint was possible to almost a normal amount. In the forefinger motion was limited by the old ankylosis. In the middle finger there was no flexion at the distal joint, suggesting proba-

ble separation of the suture line of the deep tendon, or possibly fusion of the tendons. There was great weakness of the adductors of the thumb with atrophy in this area. There was hypesthesia to pin-prick over a portion of the palmar surface of the middle finger (fig. 5).

In addition to the abnormality in the tendons it was felt that this patient presented evidence of traumatic vasospasm, and he was admitted to the hospital for study.

Immersion of the two hands in ice-water showed a marked delay in the return of surface temperature in the left hand (fig. 6). An ergometer devised by the department of physiology for measuring the strength of the adductors of the thumb showed that on the left side these muscles had 20 per cent of the strength of the corresponding muscles on the right side (fig. 7). The patient was then given 50,000,000 killed typhoid bacilli intravenously, with a slight rise in the body temperature (fig. 7). During the course of this slight fever the strength of the adductors was almost doubled. The following day a similar dose of 75,000,000

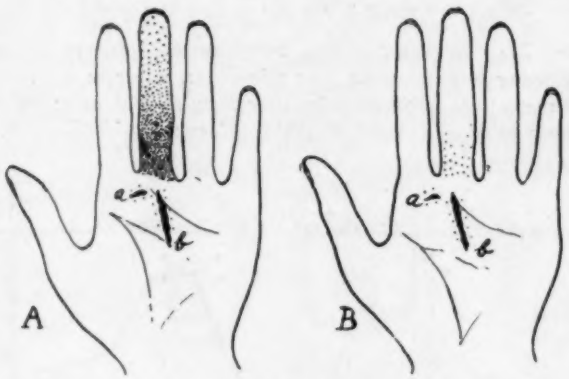

Fig. 5 (case 2).—*A*, sensory loss preceding, and *B*, following, induced fever. Note the unanatomic distribution of sensory loss and its almost complete disappearance three days later, following the induced fever. Note that neither the accidental, *a*, nor the surgical wound, *b*, could involve the motor fibers to the adductors of the thumb. The degree of hypesthesia is shown by the intensity of the stippling.

organisms was given (fig. 7), following which there was a chill and a maximum oral temperature of 103.4 F. During the course of this fever the strength of the adductors went up from 1½ pounds (0.7 Kg.) to 2¾ pounds (1.2 Kg.), almost triple the strength of these muscles on admission. The morning after this fever, when the temperature was again approximately normal, a remarkable change was observed in the hand. The hypesthesia of the finger had almost completely disappeared (fig. 5), and the limitation of extension was gone. The latter had at first been thought to be due to a contraction of scar tissue, but this observation showed definitely that its origin lay in muscular spasm in the forearm or hand which was released by sympathetic paralysis. In addition the response of the surface temperature to immersion of the hands in ice-water showed a definite approximation of the curve for the diseased side to that of the normal side (fig. 8). The strength of the adductors had returned almost to the original level (fig. 7).

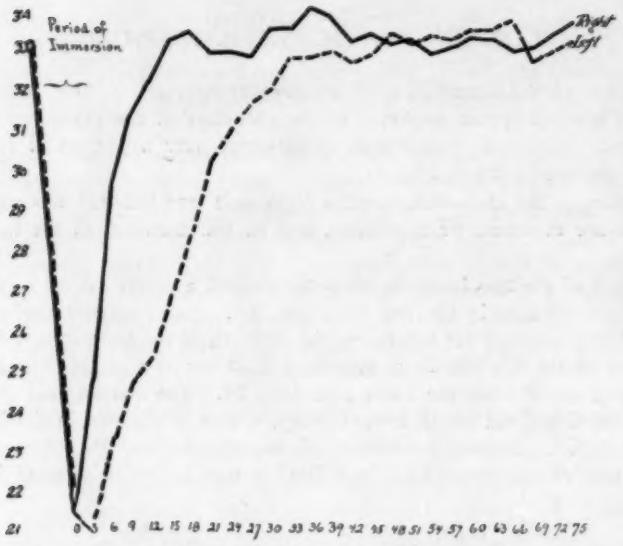

Fig. 6 (case 2).—Curve for surface temperature of fingers of the right and left hands, following immersion for four minutes in water at 0 C. The diseased hand does not reach the control level for over forty-five minutes; the normal hand does so in fifteen minutes (March 9, 1933). Compare with figure 8.

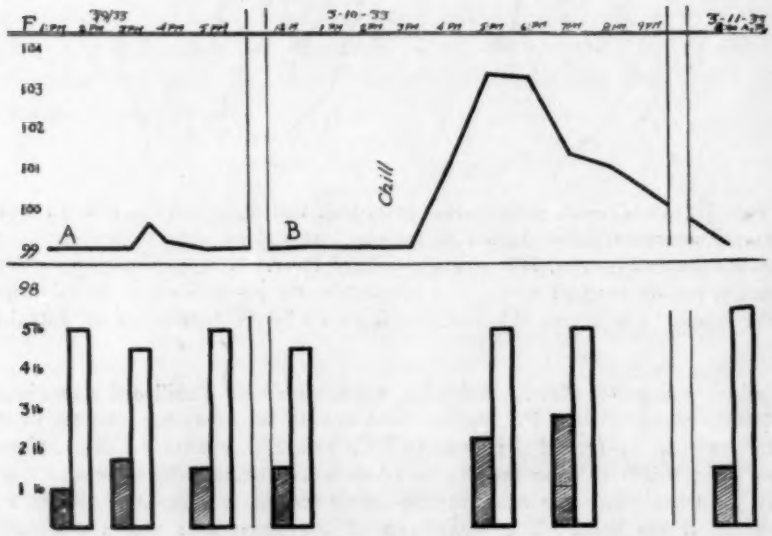

Fig. 7 (case 2).—Ergometer readings (thumb adductors) plotted against oral temperature in induced fever. Note that with the slight rise in temperature on March 9 the pull of these muscles is increased 75 per cent and that at the height of the fever on the next day it is increased 175 per cent. On the third day it remains 50 per cent above the original level. *A*, chart for temperature following intravenous inoculation with 50,000,000 typhoid bacilli. *B*, chart for temperature following inoculation with 75,000,000 typhoid bacilli. The shaded areas represent the ergometer readings for the diseased hand; the white areas, the readings for the normal hand.

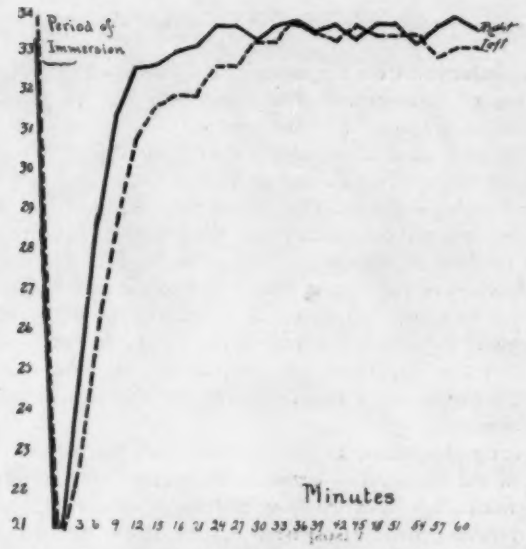

Fig. 8 (case 2).—Curve for surface temperature of the fingers of the right and left hands following immersion for four minutes in water at 0 C. These readings were made twenty-four hours after a rise in temperature following inoculation with typhoid vaccine. Note that the curve for the diseased hand approaches that for the normal hand on the day following the induced fever (March 11, 1933). Compare with figure 6.

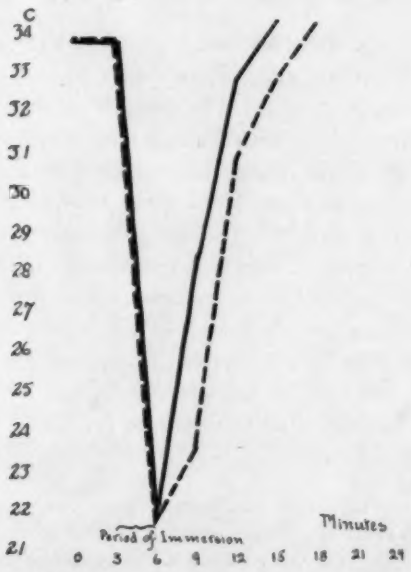

Fig. 9 (case 2).—Curve for surface temperature of finger of the right and left hands following immersion for three minutes in water at 0 C. This test was made two months after that shown in figure 8.

The patient was discharged from the hospital and instructed to return for physical therapy, consisting of massage and diathermy. He was to report for further study and decision on exploration of the tendons.

Nearly two months later after many efforts, the patient was brought back to the hospital. An examination showed no further evidence of the changes which had been observed on his first admission, except that the forefinger and the middle finger were in the original condition. The hand was no longer blue, moist or cool, there were no sensory changes, and the strength of the adductors was equal to that of the adductors of the normal hand. Atrophy was completely absent; the thenar eminences were equal in volume. As softening of the operative scar permitted more adequate palpation, it appeared likely that the tendons were tied up in scar tissue rather than separated. A chart of the reactions to cold water was obtained (fig. 9), showing still a slight delay in the return of surface temperature on the involved side.

The most striking observation at this time was that the patient found his hand entirely useful and did not want to consider the problem of operation on the tendons. In other words, the most disabling portion of his disturbance in function was the portion resulting from vasospasm, in spite of the fact that the flexion of one finger was entirely lost. Unquestionably a part of the explanation for this phenomenon lay in the fact that he had previously accustomed himself to an ankylosed forefinger so that the additional loss of flexion of the adjoining finger was relatively unnoticed.

When the patient was seen last on June 16, 1933, there was beginning subluxation at the proximal interphalangeal joint, owing unquestionably to the pull of the interossei. It is probable that the patient should now have exploration of the tendons, although I should be disposed to repeat the artificial fever once more before operating, in view of the recent reaction to cold.

There is little doubt that this case represents a degree of sympathetic irritation, with vasospasm and sensory and motor disturbances comparable to those seen in case 1. The time of onset of the sympathetic symptoms is not clear. The question may be raised as to whether disturbances in healing of the tendon after suture may not have been due to early circulatory disturbance from this underlying sympathetic malfunction. Certainly it seemed meddlesome to attempt ordinary reparative surgical procedures on this crippled hand until all evidence of sympathetic disturbance had been removed. The degree to which sympathetic dysfunction alone can cripple an extremity is particularly emphasized by this case. The hand was useless to the patient while vasospasm was present and became entirely useful when vasospasm was absent, in spite of the fact that two fingers remained without flexion at the interphalangeal joints.

CASE 3.—*Superficial puncture wound of the elbow. One month later, increasing awkwardness and weakness of the hand with sensation of coolness. Hand objectively pale and cool. No vasomotor studies. Excision of chronic inflammatory nodule over olecranon. Complete relief of symptoms. Pathologic report: chronic inflammation with perivascular infiltration.*

In A. R. P., an unusually intelligent and well educated white woman, aged 45, a rose thorn penetrated the right elbow just below the olecranon. An immediate

Fig. 10 (case 3).—Photomicrograph of nodule excised from superficial tissues over olecranon. Chronic inflammation and perivascular infiltration.

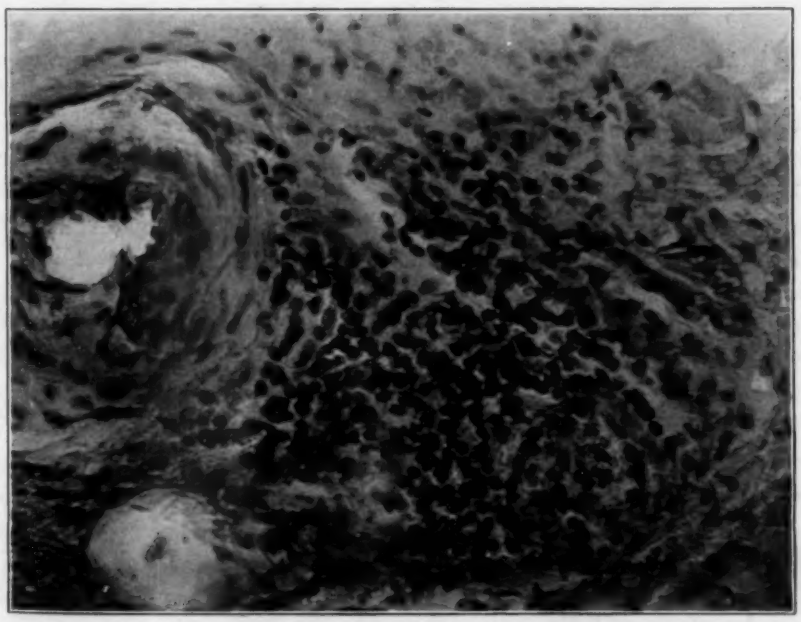

Fig. 11 (case 3).—Same as figure 9. Higher magnification to demonstrate inflammatory lesion involving the coats of a small artery, a possible source of sympathetic irritation.

unsuccessful search for a foreign body in the skin was made by a physician, with the aid of a lens. The spot of entrance of the thorn remained tender, and a nodule developed.

The patient was a successful author who set herself a regular task of composition for four hours daily. She was right-handed and did not employ the typewriter or dictation. She was seen about four weeks after the injury.

Recently the hand had not felt normal. It had been somewhat awkward and had tired easily. It felt cold. The patient expressed it by saying "it feels as though the circulation is not right."

The examination showed at the point of injury, a small, slightly tender black dot in the skin that could barely be seen. Underlying this was a nodule about 3 mm. in diameter. There was no redness or heat. The right hand was slightly paler and cooler than the left. No objective observations as to surface temperature were made.

A diagnosis of sympathetic vasospasm from perivascular irritation from a foreign body was thought possible, and excision of the nodule was advised.

Under local anesthesia the nodule was excised down to the deep fascia including surrounding fat. A small artery was demonstrated entering the area of inflammatory tissue. This observation is of interest in relation to the possibility of disturbance of the sympathetic nervous system.

The wound healed cleanly. There was practically immediate return of normal sensation and function in the hand and arm, which has remained normal since. The pathologic diagnosis was: "section of skin showing chronic inflammation, perivascular infiltration and vacuolization" (figs. 10 and 11). No foreign body was present.

This case shows in a very minor degree the elements that one must recognize as being present in major degree in the other cases detailed. There is no proof that this relatively slight disturbance is sympathetic in origin or that it may not be entirely explained on a psychic basis. The sequence, however, of injury in the neighborhood of a vessel, coolness and dysfunction in the extremity, pathologic demonstration of perivascular inflammation, and immediate complete disappearance of symptoms following removal of the limited area in which the inflammation is present, is logical and orderly to a degree. If one assumes, then, that this case represents a slightly developed instance of the conditions under discussion, it has particular interest from several points of view. In the first place, the condition was diagnosed and successfully treated at an exceedingly early stage. In the second place, the treatment was unusual in that the focus of sympathetic irritation could be completely ablated. In the third place, the pathologic picture of changes that may produce sympathetic irritation is furnished for study. Lastly, these pathologic changes are strikingly similar to those in the case of sympathetic malfunction about to be presented.

CASE 4.—*Puncture wound of right forearm. Twelve months of treatment as infection. Complete disability of upper arm, forearm and hand. Continuous pain. Marked doughy swelling. Coolness. Amputation considered. Brachial periarterial sympathectomy. Cure.*

D. E. D., a white schoolgirl, aged 18, first entered the hospital on Feb. 27, 1929, complaining of a painful, useless right hand following a wound in the right forearm. Four months previously a crabapple thorn had penetrated the ulnar border of the right forearm. Two days later the whole forearm became red, swollen and painful. She had had several incisions with the placing of drains after pus was obtained.

On admission the following description of her condition was made: "The lower part of the right arm is held by the left hand for fear of hurting it. The patient can move the right wrist only a little, can move the fingers only with difficulty and has no grip in the right hand. The arm cannot be pronated. There is a small draining sinus in the forearm in the middle third from which whitish pus exudes. There are induration, swelling, redness, tenderness and local heat surrounding the sinus as well as halfway to the elbow and wrist. The sinus leads down to the ulna, but no bare bone was made out. No epitrochlear or axillary glands were felt."

A diagnosis of retained foreign body was made, and at operation two small wooden splinters were removed. A roentgenogram showed no evidence of destruction of the bone. The patient was discharged on March 3, 1929, and was readmitted on June 10, 1929. The wound of the previous operation had healed. Two months later the arm began to turn red, to swell and to become painful at the original site. The wound broke open and suppurated. On June 13, 1929, another operation for drainage was performed, but no foreign body was found, and the patient was discharged on June 16.

On July 13, she was readmitted without any permanent improvement. There had been improvement for a time, but the incisions did not heal. Later the arm again became swollen and painful. It was noted at this time that the discharge from the wound was bloody serum and not pus. An examination showed bluish discoloration of the skin surrounding the two incisions with swelling and tenderness in the forearm in this region. A note stated: "The patient cannot flex the wrist or fingers of the right hand. The right arm is lifted with effort and pain." It is notable that at this time her temperature and leukocyte count were normal. The stiffness of the right wrist and hand was ascribed to disuse.

Persistence of the idea that the continued inflammation and disability were due to a retained foreign body led to a third operation on July 20. At this time the sinus tracts were laid wide open and dissected. No improvement followed, in spite of continuous applications of wet heat, diathermy, massage, roentgen treatment and finally the application of a cast.

On August 26, another area of redness and swelling developed; this was excised. Microscopic study showed inflammation in the fat tissue, including particularly perivascular infiltration (fig. 12). The pathologic changes in this lesion were strikingly similar to those described for case 3 (figs. 10 and 11), although not different from those found in many areas of chronic inflammation. The patient was discharged on September 3, apparently slightly relieved.

She was readmitted on September 25, and I was asked to see her. The disability in the arm had become practically complete. Pain was almost continuous, requiring the use of sedatives. The arm was held flexed at an angle of 90 degrees.

The forearm was definitely tender over its entire surface. The forearm and upper part of the arm to a point ½ inch (1.2 cm.) below the border of the axilla were swollen and doughy. Two of the old incisions were healed, and one was only partially healed. The right radial and brachial arteries were less easly felt than the left. The fingers were somewhat cool.

At this time the leukocyte count was 8,720 with 65 per cent polymorphonuclear leukocytes. All the other examinations including roentgen study of the right arm failed to reveal any abnormalities. No objective measurements of surface temperature or other special studies were made.

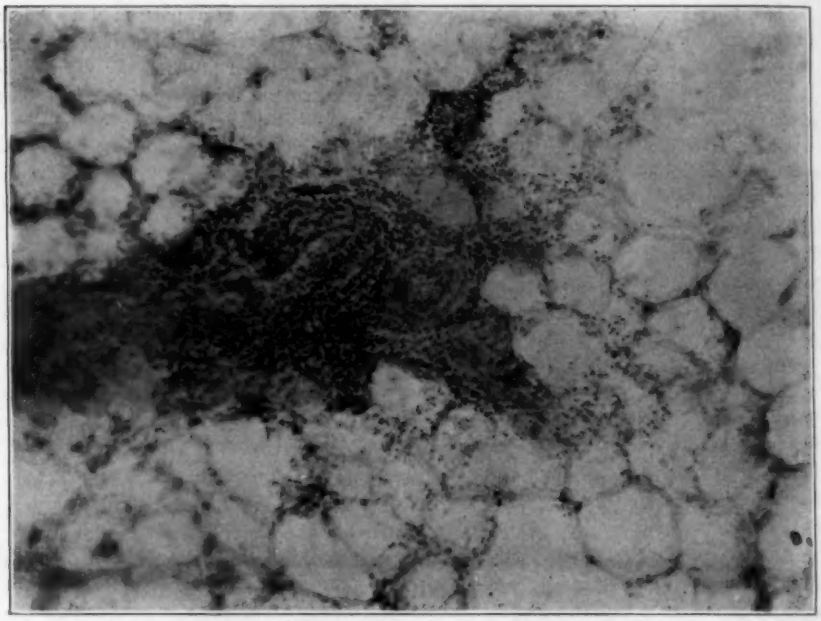

Fig. 12 (case 4).—Photomicrograph of tissue removed at the fourth operation, Aug. 26, 1929. Chronic inflammation and perivascular infiltration. The lesion resembles closely that seen in case 3, figures 10 and 11.

Before I was asked to see the patient it had been felt that the condition was hopeless and that she deserved the relief from intense suffering that amputation would offer. The condition, however, was suggestive of the rather ill defined state which was observed in injuries received in the war and called trophic edema. This was usually seen following small penetrating wounds of the type described. Certainly the choice seemed to lie between amputation and sympathectomy.

On September 28, therefore, a periarterial sympathectomy was performed on the right brachial artery with the typical primary and secondary physiologic results. The postoperative course and the healing of the wound were normal.

On September 30, the following note was made: "Patient now seems to have much better movement of the fingers than before the operation. The arm is not so tender." On October 15, the following note was made: "Flexion at elbow normal, extension to 120 degrees. Palmar and dorsal flexion of hand to about 15

degrees. The wound is healed." The hand which had been warm and dry from the time of the operation to about this date began to approach the temperature of the normal hand. The measurements of swelling before and after the operation showed an average diminution of from 1 to 2 cm. in the circumference of the arm in ten days. The patient was discharged on October 15.

She has been followed by letter and by a single visit. Improvement, begun before she left the hospital, was uninterrupted. On March 14, 1930, five and one-half months after the operation, her father wrote that the wound had healed and the hardness of the arm had disappeared, but that there was still some weakness of the fingers. On March 19, her physician wrote that the movements of the hand and arm were normal, that there was no pain, and that she was able to use the arm actively in housework, the only abnormality being the scars from earlier operations. The patient reported in person on June 14, 1932, two years and nine months after the operation. No abnormality was found except the scars, one of which was slightly attached to the ulna. The surface temperatures of the hands were equal.

This case is illustrative of two points: first, the serious loss in suffering and expense, running through an entire year, that resulted from failure to recognize the condition, and, second, the present lack of a clearcut conception of the disease from a lack of proper study before operation on the sympathetic nerves. The former needs no comment. The latter must be strongly emphasized. I have named the condition somewhat hesitantly "trophic edema." It is not at all improbable that adequate study would have enabled me to diagnose it with certainty and probably to have placed it in the group just presented, namely, that of vasospastic states following trauma. Finally, attention must again be called to the pathologic picture presented here and in the preceding case. Perivascular cellular infiltration was an outstanding element in both, furnishing an obvious mechanism for the irritation of sympathetic fibers.

This presentation illustrates several points of importance. In the first place it indicates how much information can be gained by a properly complete study of these unusual phenomena. With earlier cases, including the instance of trophic edema here reported, an adequate study of the sympathetic function of the extremity was not carried out. One can never hope to understand the curious sensory and motor effects that may be seen in disabilities of presumed sympathetic origin until in a long series of cases one can look back at objective records and detect some uniformity of behavior in relation to the supposed etiology of the condition and to the various forms of treatment exhibited. Only through the careful study of the first case here presented was a recognition of the two similar cases made possible.

The second point of importance is the recording, in as great a number as possible, of these curious states illuminated by modern methods of study and treatment, in order that they may be recognized by all practitioners in early stages. There is no doubt that in my own experience

in earlier years, a number of patients have been allowed to suffer or recover slowly without the benefit of a proper diagnosis. It is noteworthy that the case of trophic edema herein presented was called to my attention with the suggestion that amputation was indicated. This patient had had more than adequate treatment by ordinary means, faithfully followed out, with no improvement whatever. Today she is well, with an entirely useful arm which might easily have been sacrificed four years ago.

One case presented suggests the possible relationship between these states and the healing of wounds. It is essential that all physicians treating accidental wounds be on the alert for vasospastic phenomena which may come on slowly following an injury. The cool, blue, moist, perhaps painful, usually somewhat disabled hand is the danger signal. One must not be content with such expressions as the atrophy of disuse or splint stiffness until one is convinced that sympathetic impulses are not at fault.

The diagnosis of these sympathetic disturbances is not necessarily difficult, provided the sympathetic system is kept in mind. Differentiation from traumatic neurosis and hysteria is another matter. I am not entirely satisfied that in at least two of these cases the psychic factor has received sufficient attention. If anything is meant by traumatic vasospasm, however, it is probable that these cases should be so classified. One must remember that what is now called by this name was included by the earlier writers under the blanket term of vasomotor neurosis. There is, of course, a psychic element in every injury and disease. Recent studies of surface temperature reactions by the newer methods have demonstrated more and more clearly the great sensitiveness of vasomotor control to emotional stimuli. It may well be that the psychic factor is predominant in any instance of traumatic vasospasm. Looked at from this point of view the importance of differentiation between this condition and a pure hysterical reaction diminishes greatly. If traumatic vasospasm can be recognized as an entity and can be relieved by medical or surgical measures directed toward the sympathetic control of the blood supply to the extremity, the psychic element need have no more attention than the psychic element in any sick person.

It becomes necessary, therefore, only to show that a vasospastic element is present. In most instances the objective tests, which have been illustrated in the cases presented, are sufficient to accomplish this. The effect of cold on the volume flow of blood, as measured by the curve for surface temperature following immersion in ice-water, is of great value. The reaction of surface temperature and the response of symptoms to methods reducing sympathetic activity are of equal value. In the type of lesion under discussion the production of an artificial fever by typhoid vaccine is, to my mind, the method of choice. Blocking of

the sympathetic pathways by injection of procaine hydrochloride at any level will teach nothing about the relief from pain, recovery of sensory loss or improvement in somatic motor function. Its usefulness is limited to a demonstration of its effect on volume flow and sweating. Artificial fever, however, as has been illustrated herein, may furnish information of tremendous importance not only as regards the volume flow of blood but also in the field of symptomatic changes. In addition, in certain cases vasospasm can apparently be permanently released and the condition cured by artificial fever. One must, of course, be on the alert for the *post hoc* fallacy.

Lastly, the methods of treatment of the individual patient must be individualized. With methods now available, there is little doubt that in the conditions under consideration at least one or two treatments with typhoid vaccine should be tried before surgical measures are instituted. How individual the treatment may be is illustrated by case 3, in which the excision of a small superficial inflammatory nodule was all that was needed. As these cases illustrate, one is not justified in advising surgical intervention on the sympathetic system simply because the diagnosis of sympathetic disturbance has been made.

NEUROFIBROMATOSIS WITH OCULAR CHANGES AND INVOLVEMENT OF THE THORACIC SPINE

REPORT OF A CASE

M. M. COPELAND, M.D.

L. F. CRAVER, M.D.

AND

A. B. REESE, M.D.

NEW YORK

Pigmentation of the skin and multiple neurofibromas are characteristic of Recklinghausen's disease, but numerous other manifestations are seen.[1]

Changes in the bone have been observed in cases of neurofibromatosis. Brooks and Lehman,[2] Castronuovo,[3] Camp,[4] Camp, Adson and Shugrue,[5] Gould,[6] Weiss,[7] Adrian,[8] and Stalmann [9] reported cases with various associated changes in the bone, including scoliosis, abnormality of growth, irregularity of outline, central and subperiosteal cysts, pedunculated subperiosteal tumors and pseudo-arthrosis.

From the Memorial Hospital.

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Siegmund [10] reported a case of neurofibromatosis with bony cavities of the lumbar and sacral vertebrae lined by herniations of the dura and accompanied by aneurysmal dilatations of vertebral arteries.

Ocular changes associated with Recklinghausen's disease are also recorded. Goldstein and Wexler [11] described a case of melanotic tumors of the iris with orbital neurofibromas and called attention to the frequent occurrence of orbital neurofibromatosis accompanied by pigmented nevi of the lids, conjunctiva and sclera, hydrophthalmos, buphthalmos, elephantiasis of the lids and melanosis of the uveal tract and iris.

The following case presents features of Recklinghausen's disease with extensive medullation of the nerve fiber layer of the retinas and changes of the bone in the thoracic vertebrae.

REPORT OF A CASE

M. W., a Jewish youth, aged 14, was referred to the Memorial Hospital in March, 1933, by Dr. H. Hallock, of the Orthopedic Hospital, Orange, N. J., complaining of discomfort and deformity in the upper part of the back.

The patient's father had typical coffee-colored patches in the lower lumbar region. A paternal aunt had a similar spot over the right shoulder.

At birth the boy had what was called a large brown mole on the back. As he grew older, various pigmented areas appeared over the body. Development seemed to be normal in every other respect.

Two years before admission to the hospital he began to experience pain in the upper posterior thoracic region and lassitude, especially in the evening. One year later his mother noticed a deformity of the thoracic spine.

Physical examination on admission revealed a fairly well nourished youth.

A special examination of the eyes by Dr. A. B. Reese showed the palpebral apertures to be of equal size; the exophthalmometer reading was 19 mm. for each eye. No masses were palpable in the orbits. The lids were normal. The extraocular movements were normal. The pupils were equal and regular; they reacted to light and in accommodation both directly and consensually. Slit-lamp examination gave negative results. Ophthalmoscopic examination showed extensive medullation of the nerve fiber layer of the retina in both eyes. In the right eye the medullation completely surrounded the disks and extended into the retina for 2 disk diameters above and below, while temporally and nasally it extended only 1 disk diameter. In the left eye there was no medullation of the fiber layer temporally and nasally to the disk, but above and below it extended for 1 disk diameter. The examination of the fundus of the eyes with widely dilated pupils otherwise gave entirely negative results.

The fields of vision were taken on the Ferree-Rand perimeter under standard illumination with a 5 mm. test object. They were of normal limits. The blind spots, taken on the tangent screen with a 5 mm. test object, were normal.

There was slightly reduced vision in the right eye. This was attributed to amblyopia exanopsia, as the patient had considerable hyperopia and esophoria with a history of slight esotropia.

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10. Siegmund: München. med. Wchnschr. **90**:28, 1930.

11. Goldstein, I., and Wexler, D.: Melanosis Uveae and Melanoma of the Iris in Neurofibromatosis, Arch. Ophth. **3**:288 (March) 1930.

The intra-oral cavity showed poor approximation of the teeth; otherwise it was normal. There was moderate adenopathy in the neck.

Examination of the chest showed a markedly keel-like thorax. There was a rotation of the upper thoracic vertebrae toward the right, and a displacement of the ribs backward on the right. Kyphosis and right scoliosis existed in this region. There was slight tenderness definitely localized over the upper dorsal vertebrae. An extensive area of pigmentation was found over the back (fig. 1). Several smaller areas of pigment covered the anterior part of the chest and arms.

Fig. 1.—Note the extensive areas of pigmentation. The right scoliosis of the spine can be seen with displacement of the right scapula and ribs backward.

The heart and lungs were normal.

The abdomen also was covered with small areas of coffee-ground spots. The spleen was just palpable. No other masses were felt in the abdomen.

Examination of the genitalia showed pigmentation of the glans penis; the testes were normal. Rectal examination gave negative results.

On the lateral surface of the left hip, at about its midportion, was a small subcutaneous mass, suggesting a neurofibroma. The legs showed a wide distribution of Recklinghausen's pigment. No other subcutaneous masses were felt over the body.

Roentgenographic studies of the chest and spine showed marked right lateral scoliosis of the upper dorsal region. The bodies of the vetebrae in the scoliotic

region were wedge-shaped as a result of slight destruction, and the ribs in this vicinity showed multiple small areas of diminished density representing destruction of bone. All of these findings were in accord with the clinical diagnosis of neurofibromatosis.

The blood of the patient was studied for its intermedin content by Dr. Russell Ferguson. The intermedin was extracted from the blood and injected into Elritze fish (Phoxinus laevis), which were used as test objects. The blood was found to have 334 phoxinus units of intermedin per liter.

When last seen the patient showed no other changes clinically. He had been advised to refrain from strenuous exercise and was under close observation.

Fig. 2.—Roentgenogram showing right lateral scoliosis in the upper dorsal region. The bodies of the vertebrae are wedge-shaped as a result of slight destruction. The ribs in the vicinity show multiple areas of rarefaction due to changes in pressure.

COMMENT

Neurofibromas arise from spinal nerve roots as well as from the peripheral nerves. They may be intrameningeal or extrameningeal or extend along the course of the nerve. The extrameningeal portion may erode through the intervertebral foramen to form extravertebral masses. In the region of the thorax and abdomen they usually produce massive erosion of all of the adjacent bony structures.

Camp [4] of the Mayo Clinic found that between the years 1930 and 1932, inclusive, 23 per cent of all tumors of the spinal cord operated on were neurofibromas. He also found that 42 per cent of the cases showed osseous changes.

The bone is involved usually by direct pressure from erosion, and the defect observed in roentgenograms coincides with the site of the tumor. The roentgenographic changes are usually erosion and thinning of the vertebrae and their processes. Change in the contour of the vertebrae is a late manifestation. As the tumor increases in size, evidence of erosion of the ribs is seen. The discovery of a tumor extending along nerve roots and penetrating through the intervertebral foramina causing changes of the bone in this area should suggest the presence of a neurofibroma.

Medullated nerve fibers occurring in the retina have been found in cases of Recklinghausen's disease. In a study of 12 patients with neurofibromatosis, Fischer [12] found retinal medullated nerve fibers 4 times. He is inclined to the view that the incidence of medullated nerve fibers in the retina is greater among patients who show definite abnormalities in the central nervous system or have psychopathic disturbances. In a routine examination of the eyes of 3,250 patients Manz [13] found 1 patient with medullated retinal nerve fibers, while in an examination of 130 inmates of an asylum he found its occurrence 4 times.

The retinal medullated nerve fibers appear normal histologically when compared with medullated fibers [12] in nerves usually containing them.

In a personal communication Ferguson [14] stated that intermedin (the melanophore-expanding hormone of the pituitary) was found in the blood in 8 proved cases of melanoma and 1 case of neurogenic sarcoma besides our case of Recklinghausen's disease. He feels that it may be possible to find a fundamental relationship on a quantitative basis between melanoma, neurogenic sarcoma and neurofibromatosis. Such a finding would lend biologic support to Masson's theory and help exclude from this relationship tumors which do not arise from the chromatophore cells of the nerve sheaths or end-organs.

This case emphasizes the vertebral changes and ocular findings which may be associated with neurofibromatosis. The finding of intermedin in the blood is of interest and may lend biologic support to Masson's theory of the association of the chromatophore cell in the nerve sheaths and end-organs with Recklinghausen's disease.

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12. Fischer, H.: Contributions to Recklinghausen's Disease; Anomalies of the Eye, Particularly the Medullary Nerve Fibers of the Retina, Dermat. Ztschr. **42**: 143, 1924-1925.

13. Manz, quoted by Fischer.[12]

14. Ferguson, R. S., and Hilderbrand, G. E.: Preliminary Note on the Occurrence of Intermedin in Melanoma and Related Conditions, Am. J. Cancer, to be published.

RETROPERITONEAL PERIRENAL LYMPHANGIOMA

HERMAN L. KRETSCHMER, M.D.
Urologist, Presbyterian Hospital
AND
WILLIAM G. HIBBS, M.D.
Pathologist, Children's Memorial Hospital
CHICAGO

The retroperitoneal tissues above and below the kidney may be the seat of a variety of tumors, which may be benign or malignant, cystic or solid. It is generally assumed that benign tumors and cysts occur more frequently than do malignant growths, and that solid tumors are more commonly seen than the cystic type.

Gobell (1901) collected reports from the literature of 101 cases of retroperitoneal tumors, which he divided into the following groups:

	Cases
Benign retroperitoneal growths	43
Malignant retroperitoneal growths	32
Either type of retroperitoneal growths	14
Retroperitoneal cysts	12
	101

No case of retroperitoneal lymphangioma is found in Gobell's collection of cases.

Mauclaire (1910) studied tumors of the retroperitoneal space and described about the same varieties as Gobell did. Magoun (1919) reported a series of 73 retroperitoneal tumors, 53 of which were operated on, 29 proving malignant, while 18 were benign; the nature of 6 was not determined. Having recently had the opportunity of studying a rare type of retroperitoneal tumor we report the following case:

REPORT OF A CASE

History.—Mrs. J. W., aged 59, referred by Dr. R. C. Brown, was admitted to the Presbyterian Hospital on Oct. 14, 1928. The patient gave a history of nocturia and mild frequency about eight years before admission. Since then she had had an ache in the right upper quadrant of the abdomen. Various physicians told her that she had an enlarged right lobe of the liver. She had never had jaundice or an acute pain in the right upper quadrant. For several years, she had felt a definite mass under the costal arch. When she was on her feet the mass felt heavy

Read at the Annual Meeting of the American Association of Genito-Urinary Surgeons, Washington, D. C., May 10, 1933.

and dragged down somewhat. She had been told that she had liver trouble and had been placed on various dietary regimens.

For an indefinite period the patient had also felt a strain or ache or pulling in the right flank. Several weeks before admission she experienced a feeling of strain that ran down the right side, across the inguinal region to the groin and down the right leg on the medial side.

Urinary symptoms were absent, but the patient had been troubled with constipation.

Physical Examination (by Dr. R. C. Brown).—The head, neck, heart and lungs were normal. Examination of the abdomen revealed a firm, smooth, globular mass which almost filled the entire right upper quadrant, projecting down from

Fig. 1.—Roentgenogram of the right side, showing moderate hydronephrosis with marked dilatation and clubbing of the calices.

under the costal arch. The lower border was on a level with the umbilicus, extending almost to the midline. On deep palpation the mass moved down in such a way that it became readily palpable bimanually. Some tenderness was present over the lower pole of the mass. The liver, spleen and left kidney were not palpable. The genitalia were normal. Examination revealed normal reflexes.

Laboratory Observations.—A blood count showed: red blood cells, 5,130,000; leukocytes, 8,800, and hemoglobin, 84 per cent. The blood pressure was 124 systolic and 80 diastolic. Urinalysis showed 310 leukocytes per cubic millimeter of fluid from the bladder, 260 from the right kidney and none from the left kidney. Cultures were sterile, and inoculations of guinea-pigs gave negative results for tubercle bacilli. A roentgen examination on October 15 revealed no change in the bones and no calculi. A cholecystogram revealed a normal organ.

Cystoscopy disclosed a normal bladder. The left ureter was catheterized without difficulty or obstruction. On the right side the catheter met an obstruction about 2 cm. from the orifice, which was overcome with some difficulty.

A pyelogram of the right kidney showed moderate hydronephrosis, with marked dilatation and clubbing of the calices (fig. 1). A pyelogram of the left kidney showed it to be normal.

Course.—From the findings a diagnosis of tumor of the right kidney was made, and operation was advised.

Nephrectomy on the right side was done by one of us (H. L. K.) on October 26, with ethylene-ether anesthesia. There was an uneventful convalescence and the patient was discharged from the hospital on November 16.

Examination of Specimen (W. G. H.).—The gross specimen consisted of the upper and medial two thirds of the right kidney to which was attached, laterally and to its lower pole, a firm semispherical, encapsulated mass measuring 8.5 by 11 by

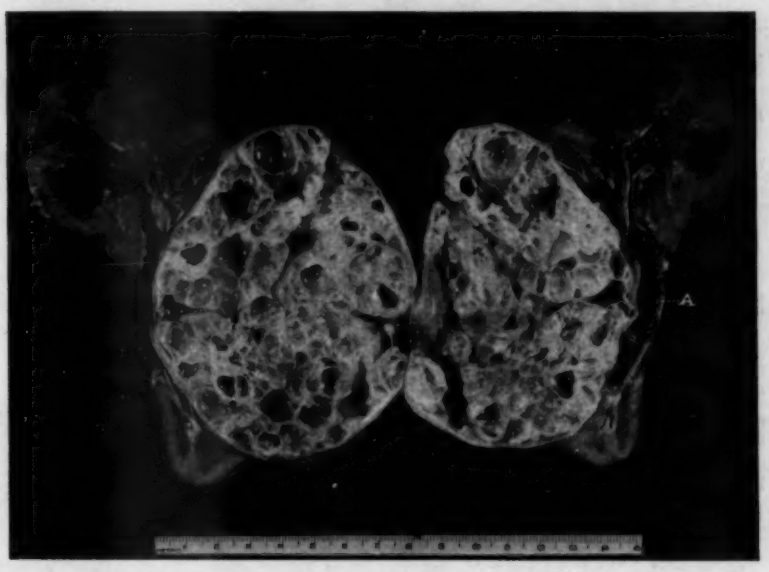

Fig. 2.—Photograph showing the sharp line of demarcation between the kidney and the tumor; *A*, the dilated renal pelvis. The cystic structure of the tumor is notable.

9 cm. The complete specimen weighed 395 Gm., and measured 14 by 10.5 by 10 cm. The tumor of the lower portion of the kidney was about four fifths of the entire specimen.

On the surfaces made by sectioning, the color of the renal tissue was normal. The cortex was from 6 to 8 mm. thick; it had well defined striations and was clearly in contrast with the medullary portion. The renal substance of the upper pole was from 8 to 15 mm. thick. Here the capsule stripped easily leaving a smooth surface.

From the upper pole the renal tissue thinned on the outer surface to blend with the capsule of the tumor mass. The renal tissue was sharply defined from the tumor by a firm capsule 1 mm. thick (fig. 2). The tissue of the tumor within its capsule had replaced the lower pole of the kidney and had been compressed up and medially into the remaining portion of the kidney.

The tumor tissue, wherever it was cut, consisted uniformly of hundreds of separate cysts with firm, thin, gray walls, which varied in size from 2 to 10 mm. in diameter. The cysts generally contained clear pale brown fluid, but in isolated places, after fixation with a solution of formaldehyde the content appeared as a firm, clear, gelatin-like substance which occasionally, in its center, contained a homogeneous opaque, yellow-brown material. In a few places in which the capsule was not adherent, the cysts occurred in clusters of eight or ten. They extended from the main mass of the tumor, which was firmly compressed within the rigid capsule. The cysts were not present anywhere within the substance of the kidney.

Microscopically the tumor consisted of simple cysts of many sizes. All the cysts were lined with a single layer of flat, broad endothelium and contained lymph (fig. 4). The endothelial cells were more than one layer thick only in isolated places. These places were at the site of a clump of smaller cysts, evidently

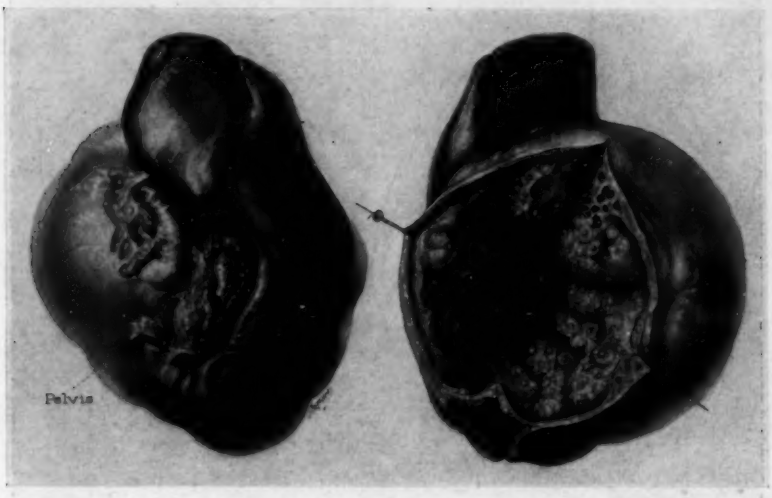

Fig. 3.—The thick capsule of the tumor is made up of hundreds of separate cysts with a firm, thin, gray wall.

at a point of compression by adjacent cysts. The amount of lymph in the compressed cyst was scant, and the hyperplastic endothelium was in the recesses of the cyst and consisted of stratified cuboid endothelium proliferating centrally into the cyst from the cells of the peripheral lining.

The walls of the larger cysts were thin, so that the space between the endothelial lining of the adjacent cysts was a delicate band of fibrous reticular tissue. Elsewhere, however, the endothelial linings of adjacent cysts were separated by dense fibrous reticular tissue in which blood vessels were sparse. In places this fibrous reticulum occupied all of a low power field, and its central portion showed few nuclei, with compression atrophy, degeneration of hyalin and isolated deposition of calcium.

The entire tumor mass, which consisted of lymphatic spaces, was separated from the kidney substance proper by a capsule of dense fibrous tissue (fig. 5). Occasionally the capsule retained isolated renal tubules which were in various stages of atrophy.

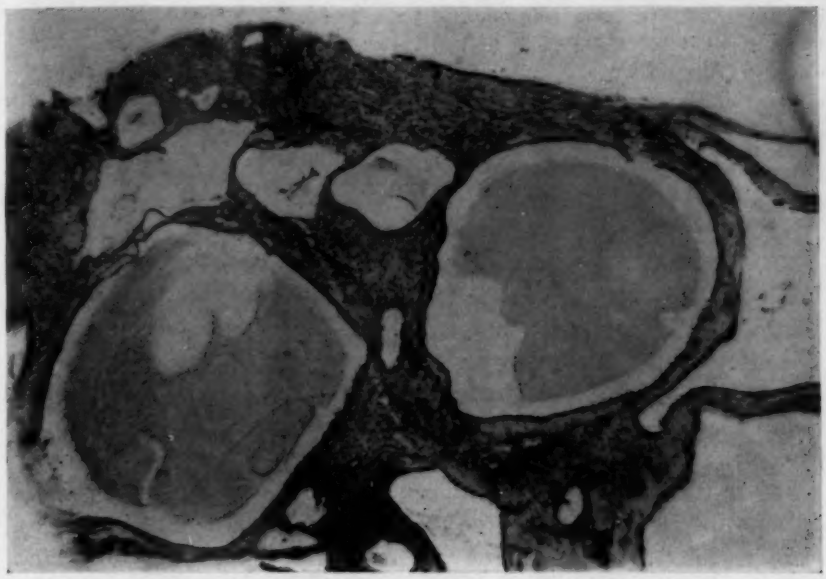

Fig. 4.—Photograph showing lymph cysts of variable size typical of the entire tumor.

Fig. 5.—The fibrous wall of the cyst contains solitary cysts with compression of the kidney. Lymphocytic infiltration is evident.

In the kidney, where the tumor had compressed it was a dense infiltration of lymphocytes. The renal substance adjacent to the capsule of the tumor was atrophic, the tubules stained poorly, and many glomeruli were hyalinized. This change of the renal tissue occurred only in that part which was adjacent to the tumor. The tissue of the kidney proper was free from histologic evidence of disease. Cysts were not present anywhere within the substance of the kidney.

REVIEW OF THE LITERATURE

The literature on the subject of retroperitoneal lymphangioma is extremely scanty. In the reviews of retroperitoneal tumors by Gobell (1901), Mauclaire (1901), Magoun (1919), Andrews (1923) and Schmid (1923), no mention was made of this type of neoplasm. In his review of the literature relative to pararenal tumors Lecêne (1919) included 1 lymphangiosarcoma (Lund, 1901) in the series of 113 cases. Gaudier and Gorse (1913) reported a retroperitoneal cystic lymphangioma, and drew attention to the fact that a diligent search of the literature revealed no strictly analogous case. They reviewed, however, the cases of retroperitoneal lymphatic cysts reported by Kilian (1886), Narath (1886), Winter (1895) and Penkert (1902), owing to the fact that these cysts showed some points of similarity to those in their own case.

Westman (1925) reported a retroperitoneal lymphangioma, which was retrocecal. He mentioned no similar case in the literature. Burhaneddin (1931) reported a multilocular cystic retroperitoneal lymphangioma, his comment being that he had not succeeded in finding a similar case in the literature. McFadden (1931) reported a successful removal of a multilocular cystic retroperitoneal lymphangioma by operation.

While there are a number of cases of chylous and lymphatic cysts reported, the 4 cases mentioned constitute the only instances of true retroperitoneal lymphangioma of which we are able to find a record. These, with the addition of the tumor herein reported, furnish 5 such cases for study.

Our survey leads us to concur with the opinion of McFadden who feels that many of the retroperitoneal cysts described in the literature were probably true lymphangiomas and not cysts arising from local peritoneal cells derived from the urogenital ridge. We include in our study, however, only those cases in which the growths were proved by microscopic study to be true neoplasms of the type of lymphangioma. Kaufmann emphasized the necessity of differentiating between lymphangioma, a new growth, and lymphangiectasis, a simple dilatation of the lymphatic vessels.

Cases of Retroperitoneal Perirenal Lymphangioma Reported in the Literature

Author	Age, Years	Sex	Duration of Symptoms	Symptoms	Clinical Diagnosis	Method of Diagnosis	Location of Tumor	Size of Tumor, Cm.	Treatment	Outcome	Comment
Gaudier and Gorse..... (1913)	4	M	.....	Inguinoscrotal tumor (fluctuant), pressure on which transmitted to the right lateral abdominal wall	Cystic abdominoscrotal tumor	Operation and examination of specimen	Right retroperitoneal region from lower pole of kidney to pelvis with extension into inguinal region	25 by 10 by 12	Surgical extirpation	Good	Tumor showed a finger-like extension into scrotum
Westman..... (1925)	58	M	About 24 hours	Tenderness over right side of abdomen, pain in right side of abdomen, nausea and vomiting	Acute appendicitis	Operation and autopsy	Retrocecal, surrounding cecum and appendix	Size of fist	Exploratory operation	Death from gangrenous appendical abscess	Tumor prevented removal of appendix, and this caused death
McFadden..... (1931)	5	M	4 years; 4 days	Enlarged abdomen, acute abdominal pain and distention with pushing out of umbilicus	Inflamed appendix or inflamed gland of tuberculous peritonitis	Operation and examination of specimen	Retroperitoneal, extending from lower pole of right kidney to inferior surface of the liver	.....	(1) Drainage of cyst; (2) extirpation of tumor 15 months later	Good	
Burhaneddin..... (1931)	40	M	3 years	Tumor, size of a fist above right inguinal fold, which enlarged to reach right costal arch	Inoperable sarcoma	Operation and histologic study of specimen	Right retroperitoneal region, bulging into abdomen and displacing cecum and appendix	45 by 35; weight, 6.4 Kg.	Excision by abdominal route (pararectal incision)	Good	
Kretschmer and Hibbs (1933)	59	F	8 years; several years	Pain in right upper quadrant of abdomen, mass which almost filled entire right upper quadrant of abdomen	Tumor of right kidney	Operation and histologic study of specimen	Attached to lower pole of kidney	8.5 by 11 by 9	Nephrectomy	Recovery	

ETIOLOGY

In considering the etiology of retroperitoneal lymphangioma careful distinction must be made between retroperitoneal and mesenteric cysts and true lymphangioma. According to Ewing, retroperitoneal lymphangioma occurs in children and adults as a multilocular cavernous and cystic tumor, originating along the spinal column and ramifying into the pelvis behind the kidney or colon, upward to the liver and the spleen and into the omentum. He stated that "the very early stages and exact origin of these tumors have not been demonstrated," and added that their neoplastic nature seems assured "since the walls contain cellular connective tissue, often much smooth muscle and lymph-follicles."

Magoun's opinion is that the origin of retroperitoneal tumors "is at the best a matter of speculation. All types of tissue are in the retroperitoneal space and may at any moment undergo abnormal growth." Harris said: "The various angiomas must have their origin in a developmental anomaly in structure of certain vascular segments which do not fit into the circulatory system, and which retain embryonal characteristics. The congenital origin of the majority of these tumors speaks strongly in favor of a tissue predisposition as a prominent factor in their genesis."

Burhaneddin mentioned the various types of retroperitoneal cysts and the theories of their etiology, but concluded that his own case was one of cystic lymphangioma—a true neoplasm. McFadden said that while its anatomic relation might have suggested the origin of his case of retroperitoneal tumor (cystic lymphangioma) from the urogenital ridge, examination revealed it to be a true lymphangioma.

The old literature contained references to lymph cysts, according to Westman. Such tumors were regarded as a result of lymph stasis, but at present they are regarded as true new growths.

Brandsburg said that the majority of lymphangiomas occur in childhood, and found that they occur with equal frequency in the two sexes. There are many theories as to their etiology, of which he enumerated four: (1) the retention theory, which explains lymphangioma on the grounds of mechanical pressure; (2) the theory of a disturbance of the secretory function of the endothelium of the vessels, causing hyperproliferation of the lymph, or a disturbance of the permeability of the endothelium; (3) the inflammatory theory; (4) the embryonal theory. Brandsburg believed that the embryonal theory is the most acceptable. It explains the lymphangioma on the grounds of a defect in the embryonal organization of the lymphatic system, small segments of tissue retaining their embryonal characteristics.

PATHOLOGY

A lymphangioma is a tumor composed of lymph vessels. It is an organoid structure consisting of endothelial cells and supporting connective tissue, both being involved in the neoplastic process.

Ewing stated that the clinical conditions which fall in the general class of lymphangioma "include a variety of slowly growing congenital single or multiple tumors of the skin, subcutaneous tissues, deep areolar structures and muscles of neck, trunk, lip, tongue, eye and orbit." He believed that in the pathogenesis of these conditions many factors are concerned; hence it is more difficult to distinguish between lymphangioma and lymphangiectasis than between true and spurious hemangioma. Ewing thought that the simple occlusion of lymph channels may be followed by extensive varicosities resembling lymphangioma. He noted that the general clinical features apparently offer an important means of recognition of lymphangioma, but even so there are a large number of investigators who would include in the class only such processes as show a congenital origin and a progressive course, with an absence of traumatic and inflammatory factors.

Kaufmann stated that on section a lymphangioma shows dilated spaces lined with endothelium, which are filled with clear or slightly cloudy lymph. The walls are fibrous and often quite muscular. The interstitial tissues contain fat and foci of lymphoid structures, and after section of the tumor the cavities collapse. Collapse of the cavities did not occur in our case. Kaufmann further stated that when the overgrowth of connective tissue is greater between the spaces, the tumor is firmer and may be termed lymphangiofibroma. He contended that in the individual case it is sometimes difficult to determine whether the mass is a true neoplasm of lymphatic vessels or only a dilatation with secondary thickening of preformed vessels with some muscular hypertrophy. A sharp differentiation should be made between lymphangiectasis (simple dilatation of lymph vessels) and lymphangioma (a new growth).

Sick (quoted by Kaufmann) believed that the starting point of many lymphangiomas is in an isolated vessel or primtive connective-tissue rest which proliferates into new lymph vessels.

In Burhaneddin's case (retroperitoneal cystic lymphangioma) the tumor was greenish white, thin walled and made up of cysts of various sizes filled with clear fluid. The tumor had no connection with the tissues around the kidney. On microscopic examination the inner walls of the cysts of Burhaneddin's tumor were seen to be lined with oblong, partly flat endothelial cells. On the external surface and in the interstices between the cysts it was noted that angiomatous tissue was developing. In isolated places the interstitial tissue showed flat, large, cellular

elements, which seemed to fill the spaces of these tissues. The diagnosis, from a study of the structure of these walls, was cystic lymphangioma.

McFadden's case revealed at operation a large cyst shaped like a horseshoe, which filled the lower part of the abdomen. In the midline it reached about an inch (2.5 cm.) above the bifurcation of the aorta, and in the flanks it extended to the pouches of both kidneys. It extended into the pelvis behind the mesosigmoid and mesorectum, was closely adherent to the perinephric fat and was tense and multilocular. In one area colonies of small cysts on the wall of the cyst gave the appearance of frog's spawn. The cysts contained turbid fluid in which were scattered flakes of lymph. Microscopic study showed the tumor to be a true lymphangioma, with a matrix mostly of fatty tissue, though in places it was fibrous with strands of plain muscle among collagen fibrils. In the matrix was a sort of spongy network of channels, some long and narrow, some in the form of wide spaces. The lining of these was a single layer of flattened endothelial cells (absent in some places), which were supported by fibrous tissues. Collections of lymphocytes were seen, sometimes in the walls of the spaces, sometimes lying irregularly in the meshes of the matrix, sometimes in spaces by themselves. Scattered foci of polymorphonuclear leukocytes gave evidence of superadded inflammatory reaction. McFadden noted the similarity of appearance of the cavernous lymphangioma to congenital hygroma of the neck or axilla.

In Westman's case the tumor surrounded the cecum on the anterior, external and posterior sides. It was the size of a clenched fist and was composed of small cysts. The growth was fixed against the posterior abdominal wall, but was easily loosened from the lower pole of the right kidney. It had no union with the appendix, intestines or other organs, and was diagnosed after microscopic study as a lymphangioma cavernosum. There was neither dilatation of lymph vessels nor any evidence of lymphostasis.

Gaudier and Gorse remarked that the pathologic process present in retroperitoneal lymphangioma is obscure. They noted that Penkert discussed the various hypotheses of degeneration of ganglions, dilatation of the lymphatic vessels and cystic degeneration of a cavernous lymphangioma. Other authors were inclined to think that the condition is a congenital malformation. Gaudier and Gorse expressed the opinion that the true explanation is wanting.

The tumor in our case, by its growth, caused pressure atrophy of the lower pole of the kidney and was attached to the kidney.

SYMPTOMS AND CLINICAL FEATURES

Retroperitoneal lymphangiomas present no clinical features which would serve to distinguish them from other retroperitoneal growths. Retroperitoneal tumors are as a rule "silent" until their size is such that symptoms of pressure arise. Burhaneddin noted that difficult respiration and ureteral pressure are two usual effects of such tumors. In his case (cystic lymphangioma) the neoplasm caused symptoms of ureteral obstruction which were relieved after removal of the mass.

In McFadden's case (retroperitoneal lymphangioma) the patient, who had had an enlarged abdomen for four years, suddenly suffered acute abdominal pain and distention of such degree that there was protrusion of the umbilicus. Palpation did not reveal a tumor, and rectal examination gave negative results. A clinical diagnosis of acute appendicitis or inflamed glands of tuberculous peritonitis was made.

The retroperitoneal lymphangioma reported by Westman had apparently caused no symptoms and was discovered incidentally during an operation for acute appendicitis. The size and position (retrocecal) of the tumor prevented the removal of the gangrenous appendix, thus causing the death of the patient in an indirect manner.

A prolongation of the tumor in the case of retroperitoneal lymphangioma recorded by Gaudier and Gorse caused an inguinoscrotal tumefaction, which served to direct attention to the growth. On examination it was noted that the pressure on the scrotum was transmitted to the right lateral abdominal wall, at which point a large, rounded, painless tumor was palpated. The clinical diagnosis was abdominoscrotal tumor of unknown nature.

In his study of retroperitoneal tumors at the Mayo Clinic, Magoun found the following to be the most prominent symptoms of the group of benign neoplasms:

Abdominal mass	15
Loss of weight and strength	10
Abdominal pain	5
Increase in size of the abdomen	2
Pain in the back	2
Bloating	1
Constipation	1
Fulness and belching	1
Paresthesia in the right leg by pressure on the growth	1

Magoun noted that these symptoms accompanied the group of malignant retroperitoneal tumors; hence he concluded that clinically it was highly improbable that one could distinguish between the types of tumor.

DIAGNOSIS

The chief aids in the diagnosis of retroperitoneal tumors are cystoscopy, ureteral catheterization and pyelography, since the differential diagnosis of retroperitoneal growths must include a consideration of renal tumor, hypernephroma, hydronephrosis, pyonephrosis and perinephritic abscess. Furthermore, consideration must be given to enlargements of the spleen, both solid and cystic tumors of the pancreas, as well as, in rare instances, to tuberculosis of the lymph nodes.

An old but simple aid in the diagnosis, namely, inflation of the colon with air, has been almost displaced by roentgenography.

When the retroperitoneal tumor occurs low in the abdomen it may be confused with lesions of the uterus or ovaries. Because of the painless nature of the enlargement, retroperitoneal tumors have led to an erroneous diagnosis of pregnancy. It is important to remember that a diagnosis of the nature of the growth, as to whether it is benign or malignant, as well as the differentiation of lymphangioma from other retroperitoneal growths, can be established only by histologic examination of the tumor.

TREATMENT

At operation for retroperitoneal tumors it is not infrequently necessary to perform a nephrectomy, as in our case, when the kidney is engulfed by the tumor, making removal of the latter without the former a mechanical impossibility. In other instances the kidney has atrophied as a result of the pressure of the neoplasm and is not worth saving, hence the importance of a thorough preoperative study of the function of both kidneys preliminary to operation for retroperitoneal tumor. The knowledge thus gained not only is important from a diagnostic point of view but may be essential during the operation, as nephrectomy may be necessary in the removal of the tumor. Hofstätter and Schnitzler noted that when bands of tissue exist between the kidney and the tumor, it is frequently impossible to tell macroscopically, during the operation, whether the bands are simple adhesions or extensions of the growth. Such a condition would predispose the surgeon to do a nephrectomy, provided he knew that the function of the opposite kidney was satisfactory. Hartmann and Lecène removed the kidney in 18 of 27 cases of pararenal tumor in which they operated.

According to Westman, Lecène, Bettman and Serby, the chief surgical difficulty in the removal of retroperitoneal growths lies in the dissection of the adhesions of the tumor to the mesentery and intestines. These authors note that in such dissection injury to mesenteric vessels may be unavoidable, and may necessitate resection of portions of the intestine. They urge that at operation for retroperitoneal tumors the surgeon and operating instruments be prepared for such an emergency.

It is generally conceded that the ideal treatment of benign retroperitoneal tumors, including the rare cystic lymphangioma, is surgical extirpation. On the other hand, Burhaneddin wrote that it is surprising that the extirpation of such large cystic tumors is frequently possible. Ours was easily removed.

Westman stated that although complete extirpation is the ideal treatment for cystic lymphangioma of the retroperitoneal regions, drainage, with tamponade and suture of the edges of the cyst to the peritoneum, may be done when the tumor is unilocular and when its size and attachments make complete extirpation impossible. He also stated that radium may be used when, for any reason, the tumor cannot be extirpated.

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PERICARDIECTOMY FOR ADVANCED PICK'S DISEASE

JOHN B. FLICK, M.D.
AND
JOHN H. GIBBON JR., M.D.
PHILADELPHIA

Despite an increasing number of reports of cases, particularly from Germany, it remained for the work of Churchill and Beck to awaken interest in this country in the surgical treatment of Pick's disease. In 1929 Churchill [1] in an excellent article on "Decortication of the Heart (Delorme) for Adhesive Pericarditis" reviewed the subject and added a successful case of his own. In 1930 Beck [2] produced Pick's syndrome in dogs by injecting surgical solution of chlorinated soda into the pericardiac cavity. He subsequently obtained a symptomatic cure in these animals by pericardiectomy. Beck also reported a successful pericardiectomy on a human being.

The pathologic physiology of concretio pericardii, or callous pericarditis, commonly known as Pick's disease, need not be discussed at length, as it has already been admirably described by Rehn,[3] Volhard and Schmieden,[4] Churchill,[1] Beck [2] and others. The essential pathologic change is a marked fibrous thickening of the pericardium which limits the normal diastolic expansion of the heart. Extrapericardiac and intrapericardiac adhesions are not an essential feature of the condition, although the latter are almost invariably present. The symptoms arise chiefly from the marked venous stasis and resemble those of chronic congestive cardiac failure. The diagnostic features are illustrated in the case reported here. The only treatment for this obvious mechanical impediment to the circulation [5] is the removal of the pericardium.

From the Surgical Service of the Pennsylvania Hospital.

1. Churchill, E. D.: Decortication of the Heart (Delorme) for Adhesive Pericarditis, Arch. Surg. **19**:1457 (Dec., pt. 2) 1929.

2. Beck, C. S., and Griswold, R. A.: Pericardiectomy in the Treatment of the Pick Syndrome, Arch. Surg. **21**:1064 (Dec., pt. 2) 1930.

3. Rehn, L.: Ueber pericardiale Verwachsungen, Med. Klin. **16**:991 (Sept. 30) 1920.

4. Volhard and Schmieden, V.: Ueber Erkennung und Behandlung der Umklammerung des Herzens durch schielige Perikarditis, Klin. Wchnschr. **2**:5 (Jan. 1) 1923.

5. Gibbon, J. H., Jr., and Churchill, E. D.: The Mechanical Influence of the Pericardium upon Cardiac Function, J. Clin. Investigation **10**:405 (June) 1931.

In the following case advanced Pick's disease was unsuccessfully treated by pericardiectomy. The failure is attributed to the presence of a thickened epicardium which was not removed at operation.

REPORT OF A CASE

History.—The patient was an Italian boy, aged 12. When he was 3 years old a mass had appeared on one side of his neck. This was incised, and a small amount of pus evacuated. The following year his parents noticed that he was not as large or as strong as his brothers and sister. In the summer of 1928, when 7 years old, he became easily fatigued on slight exertion, and his abdomen slowly increased in size. He was treated for cardiac disease by the family physician. The swelling persisted until the weather became cold, when it subsided completely. Tonsillectomy was performed at that time.

In the summer of 1929 the abdomen again became enlarged, but the swelling disappeared in the winter. In June, 1930, the swelling reappeared, and about 3,500 cc. of cloudy fluid was aspirated from the abdomen. Digitalis was given in varying amounts that summer without noticeable effect on the ascites. There was a slight puffiness under the eyes in the morning, and dyspnea on exertion when the abdomen was enlarged. Later in the summer the legs and scrotum became edematous, but following a second paracentesis of 4,000 cc. the edema disappeared.

The patient was first admitted to the Pennsylvania Hospital in November, 1930. He was then 10 years of age. He appeared undernourished, his arms and legs were thin, and his abdomen was enormously enlarged. There was no dyspnea, cyanosis or dependent edema. The veins of the neck, arms and abdomen were prominent. There was no clubbing of the fingers. The right border of the heart was 1.5 cm. from the midline in the right third interspace, and the left border 7 cm. from the midline in the left fifth interspace. The cardiac impulse was diffusely visible and palpable. There were no murmurs, and the heart sounds were of good quality. Marked ascites and a moderate-sized umbilical hernia were present. The blood pressure was 98 systolic and 72 diastolic. Four thousand cubic centimeters of clear yellow fluid, with a specific gravity of 1.018, was removed by abdominal paracentesis. No tubercle bacilli were found on smear or culture of the fluid. The liver was enlarged but not tender. The Wassermann reaction of the blood was negative, and the urine was normal, the specific gravity varying between 1.015 and 1.030. The total serum protein was 3.03 per cent; the albumin, 2.14, the globulin, 0.89, and the albumin-globulin ratio, 2.4. A roentgenogram of the chest showed an angular projection from the left side of the cardiac shadow, presumably due to an extrapericardiac adhesion. The right cardiac border was smooth. The transverse diameter of the heart was 101 mm., that of the chest, 197 mm. The patient's temperature varied between 97 and 100 F. and the pulse rate between 92 and 108. A diagnosis of cirrhosis of the liver was made. A salt-free diet was given, but the ascites recurred rapidly, and paracentesis was again necessary before his discharge from the hospital in December.

His abdomen did not require tapping again until June, 1931, when the patient was admitted to the Jefferson Hospital. Paracentesis was performed every three or four weeks in the hospital, and the fluid assumed a milky character. A guinea-pig was inoculated with the ascitic fluid, and special cultures for the tubercle bacillus were made, but no evidence of tuberculosis was found. The total protein content of the ascitic fluid varied between 3.36 and 2.19 per cent. In August, 1931, an exploratory laparotomy was performed by another surgeon. He found a smooth,

markedly thickened peritoneum, but no evidence of tuberculosis. The liver was slightly enlarged with rounded edges and had a thick white coating dotted with shallow depressions somewhat resembling the icing on a cake. The spleen was about three times the normal size, and its surface resembled that of the liver. A specimen of hepatic tissue was removed for microscopic study. It showed marked thickening of the capsule and dilatation of the sinusoids about the central efferent veins, with early necrosis of hepatic cells in that area. The lesion was similar to that observed in chronic passive congestion. There was a slight irregular fever during the patient's stay in the hospital. He was discharged in October, 1931. From that time until June, 1932, his abdomen was tapped every four weeks. Edema of the lower extremities and scrotum appeared in January, 1932, and gradually increased.

Fig. 1.—Appearance of the patient before operation. In the profile view the prominence and distention of the external jugular vein in the erect posture can be seen.

On his second admission to the Pennsylvania Hospital, June, 1932, his abdomen was enormously distended with fluid, and there were large scrotal and umbilical hernias. The legs and scrotum were edematous. The veins of the forearms, hands, feet, neck and chest were very prominent. The hands and feet were cold and cyanotic. There were moist, coarse râles at the bases of the lungs. Five thousand and five hundred cubic centimeters of fluid, containing 4 per cent protein, was removed from the abdomen. Following paracentesis the râles in the lungs disappeared. He remained in the hospital a few days and was then treated in the outpatient department. Abdominal paracentesis was necessary every two or three weeks during the summer.

He was readmitted on Oct. 14, 1932, for the purpose of confirming the diagnosis of Pick's disease, which had been suggested. The veins of the hands were unusually prominent. The external jugular veins were pulsating and distended, even in the erect posture (fig. 1). There was a definite pulsus paradoxicus. The

blood pressure was 78 systolic and 66 diastolic. The anteroposterior diameter of the chest was increased so that it assumed the barrel shape of chronic emphysema. The percussion note was resonant over the lungs. Breath sounds were vesicular and no râles were heard. Hepatic dulness began at the fifth rib in the right midclavicular line anteriorly. The lower border of the liver was easily palpable two fingerbreadths below the costal margin. The edge was rounded, and the surface smooth, firm and not tender.

There was no bulging of the precordium or visible cardiac impulse. The apex beat was not palpable. The area of cardiac dulness was slightly larger than

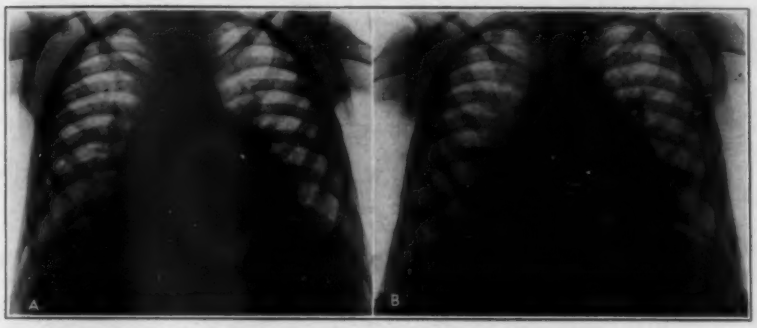

Fig. 2.—Roentgenograms of the chest, taken at a distance of 6 feet, before and after pericardiectomy: *A*, Oct. 17, 1932; *B*, Dec. 12, 1932. There is a slight increase in the cardiac area after operation.

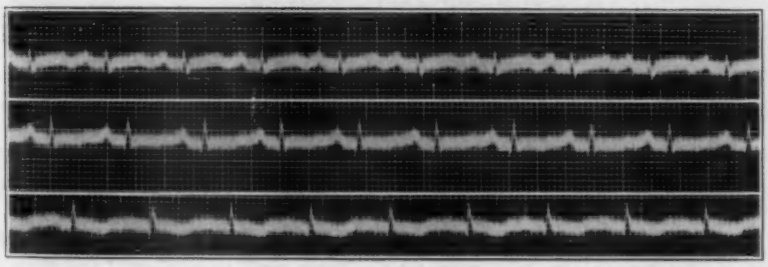

Fig. 3.—Electrocardiogram, taken on Nov. 3, 1932. No axis deviation is apparent. The Q R S complexes are slurred and of very low amplitude in all the leads. The T waves are of low amplitude in lead I, iso-electric in lead II and inverted in lead III. The resistance was 1,700 ohms.

normal. The right border was 2.5 cm. from the midline in the third interspace, and the left border, 7.5 cm. in the fifth interspace. The cardiac sounds were clear, with the exception of a slight prolongation of the first sound at the apex. There was soft pitting edema of the legs below the knees.

No cardiac pulsation could be seen on fluoroscopic examination. The cardiac outline on the roentgenogram was irregular (fig. 2 *A*). The transverse diameter of the heart was 120 mm.; that of the chest, 211 mm., representing an increase of 19 mm. in the heart and 14 mm. in the chest since November, 1930. An electrocardiogram (fig. 3) showed the very low voltage, the flat T waves, and the slur-

ring of the Q R S complex which were present in Beck's patient.[2] During October and November the venous pressure in the left median basilic vein varied between 24.5 and 22.5 cm. of water. There was no significant change in the venous pressure after paracentesis, which was performed every two or three weeks. As the history and results of the examination all indicated a far advanced and progressive case of Pick's disease, it was thought that pericardiectomy offered the only hope for improvement.

Pericardiectomy.—The operation was performed on Nov. 21, 1932. The patient was placed on the operating table with the head and chest elevated about 20 degrees. Under ether anesthesia a curved incision was made from the second left costochondral junction to the midsternal line, then down and laterally over the seventh costal cartilage. The flap of skin and of pectoralis major muscle was reflected outward. The third, fourth, fifth, sixth and seventh costal cartilages were excised. A portion of the left side of the sternum from the third to the sixth rib was removed with rongeur forceps. The posterior layer of the perichondrium of the cartilages and the exposed intercostal muscles were excised. This exposed the left internal mammary vessels, the anterior border of the left pleura and a small portion of the anterior surface of the pericardium. The pleura and the internal mammary vessels were retracted to the left and separated from the pericardium by blunt dissection. The right lung and pleura were similarly treated. At one time it was thought that the right pleural cavity had been opened, because of a "swishing" sound synchronous with respiration. The suspected area was covered with rubber dam and later with petrolatum gauze. On removal of these, at the close of the operation, no opening in the pleura was evident.

The exposed pericardium was light gray. Calcareous deposits were palpable in and beneath the pericardium, especially in the region of the right auricle. The pericardium was incised longitudinally from the pulmonary artery to the diaphragm. The heart bulged slightly through the incision. The pericardium was adherent to the epicardium throughout. It was separated from the heart by blunt dissection with the finger. In only one place, over the wall of the right ventricle, was it necessary to employ scissors to divide a calcareous band, 4 or 5 mm. thick, between the heart and the pericardium. The surface of the exposed heart was dull gray. Small, thin, calcareous plaques could be seen and felt in the thickened epicardium. These were especially numerous at the base, over the auricles and the great vessels. On palpation the sensation was that of passing the finger over coarse sandpaper. The pleural reflections were now further separated from the external surface of the pericardium. The separation was facilitated by making lateral traction on the edges of the pericardium, thus rotating the heart first to the right and then to the left. This maneuver was particularly useful in separating the right pleura from the pericardium. The anterior surface of the pericardium was then resected (fig. 4), the left side being removed first. The apex of the heart was elevated and the heart freed posteriorly. A narrow V-shaped strip was removed from the thickened diaphragmatic pericardium. There were no bands constricting the inferior vena cava.

The flap of skin and muscle was replaced over the defect in the thoracic cage, thus bringing a small portion of the right ventricle in direct contact with the under surface of the pectoralis major muscle. The wound was approximated in layers and closed without drainage. A gauze pad was firmly strapped over the wound with adhesive plaster to control the paradoxical movement of the chest wall.

The veins in the neck were still prominent at the conclusion of the operation with the patient in the semirecumbent position. The blood pressure the day before the operation was 78 systolic and 66 diastolic. Before the administration of the anesthetic on the day of the operation, it was 96 systolic and 78 diastolic; the day after the operation it was 88 systolic and 54 diastolic. The increase in the pulse pressure was maintained on subsequent readings until the patient was discharged.

There was little postoperative reaction. On the seventh day, several ounces of clear serum drained from the lower portion of the wound, spurting with the

Fig. 4.—The portions of the pericardium and the costal cartilages excised at operation.

heart beat. This drainage continued for a few days and then ceased. A superficial infection of the upper portion of the wound also occurred but subsided promptly. For three weeks after the operation there was a slight reduction in the rapidity with which the ascitic fluid accumulated. Thereafter little difference could be observed. The venous pressure was 17 cm. of water nine days after the operation, but rose to 25 cm. of water, slightly above the preoperative level, on the twentieth day. It was still impossible to observe any cardiac or aortic pulsation by fluoroscopy. There was an increase of about 4 mm. in the transverse diameter of the heart after the operation (fig. 2*B*). A postoperative electrocardiogram was essentially similar to the one taken before the operation.

The patient left the hospital on December 18, twenty-seven days after the operation. He returned on December 27 for abdominal paracentesis and was discharged the following day. The wound in the chest had healed. The veins in the neck were still prominent, the abdomen was distended, and there was pitting edema of the legs below the knees. Five thousand and five hundred cubic centimeters of fluid was removed from the abdomen.

On Jan. 6, 1933, the patient was readmitted, with marked dyspnea and cyanosis. The abdomen was distended and there was edema of both lower extremities. The

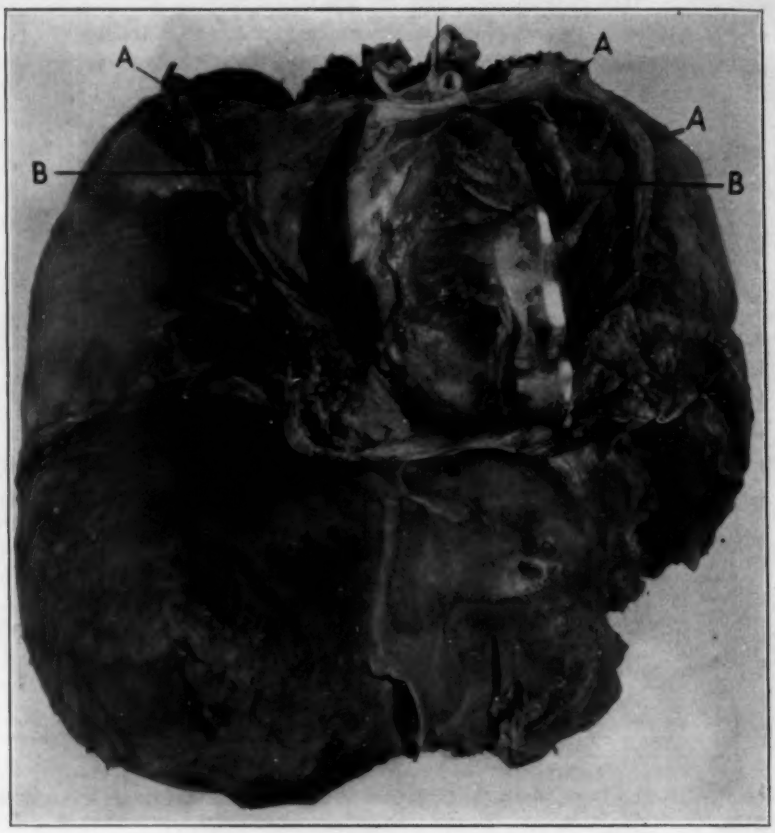

Fig. 5.—The heart, lungs and liver removed en masse at autopsy. At *A*, traction is made on the thickened pleural reflections overlying the heart. The remaining portion of the pericardium has been separated from the heart, and the line of operative resection may be seen at *BB*. The pectoralis major muscle and short segments of three costal cartilages can be seen adhering to the anterior surface of the heart. The heavy irregular deposit of fibrin dotted with shallow depressions is evident on the surface of the liver.

pulse rate was about 160 per minute and the blood pressure was 70 systolic and 50 diastolic. Shortly after admission 5,700 cc. of fluid was removed from the abdomen. Pulmonary edema developed four or five hours later, and despite stimulation and inhalation of oxygen, the patient died.

Autopsy.—Autopsy was performed eight hours after death. On opening the peritoneal cavity 2 liters of clear amber-colored fluid was removed. The peritoneum was 1.5 mm. thick, but its surface was smooth and glistening. The omentum was small and adherent to the anterior parietal peritoneum in the left upper quadrant of the abdomen. Both lobes of the liver were enlarged, extending two or three fingerbreadths below the costal margin. The entire anterolateral surface of the liver was densely adherent to the diaphragm and the parietal peritoneum. The surface of the liver was covered with a thick white mottled coating (fig. 5). The spleen was not adherent, and its capsule was similar in appearance to that of the liver. The other abdominal organs were grossly normal.

The pleural cavities were entirely obliterated by adhesions. Both pleurae were densely adherent to the pericardium. The pectoralis major muscle was firmly attached to the anterior surface of the heart where the pericardium had been

Fig. 6.—Section of the heart through the left ventricle. The epicardium has been pulled up to illustrate the plane of cleavage between it and the layer of fat lying directly on the myocardium.

removed at operation (fig. 5). The remaining portion of the parietal pericardium was again adherent to the heart, although it had been completely separated at operation. The adhesions could be separated everywhere by blunt dissection with the finger except for a dense band at the apex of the left ventricle, which had to be cut. No obstruction of the inferior and superior vena cava could be demonstrated. Even before the separation of the pericardium from the heart, the finger could be passed through the inferior vena cava into the right auricle and into the superior vena cava without meeting any obstruction or kink. The epicardium was thickened and calcified, as noted at operation. In one place the calcification extended through the left ventricular muscle to within 1 mm. of the endocardial surface. It was found that the epicardium could be stripped with comparative ease from the surface of the ventricle of the heart, from which it was generally separated by a layer of fat (fig. 6), except in places where the calcification pene-

trated through the epicardium into the cardiac muscle. The coronary vessels lay for the most part within the subepicardial fat and the myocardium and were not injured in separating the epicardium from the cardiac muscle. The borders of the mitral valves were slightly thickened and nodular at the attachment of the chordae tendineae. The width of the largest of these nodules was 3 mm. The other cardiac valves were entirely normal. The aorta was smooth and elastic, and the coronary vessels and orifices were patent and not diseased. After removal of the remaining pericardium the heart weighed 150 Gm., which is about normal for a child of this age.[6]

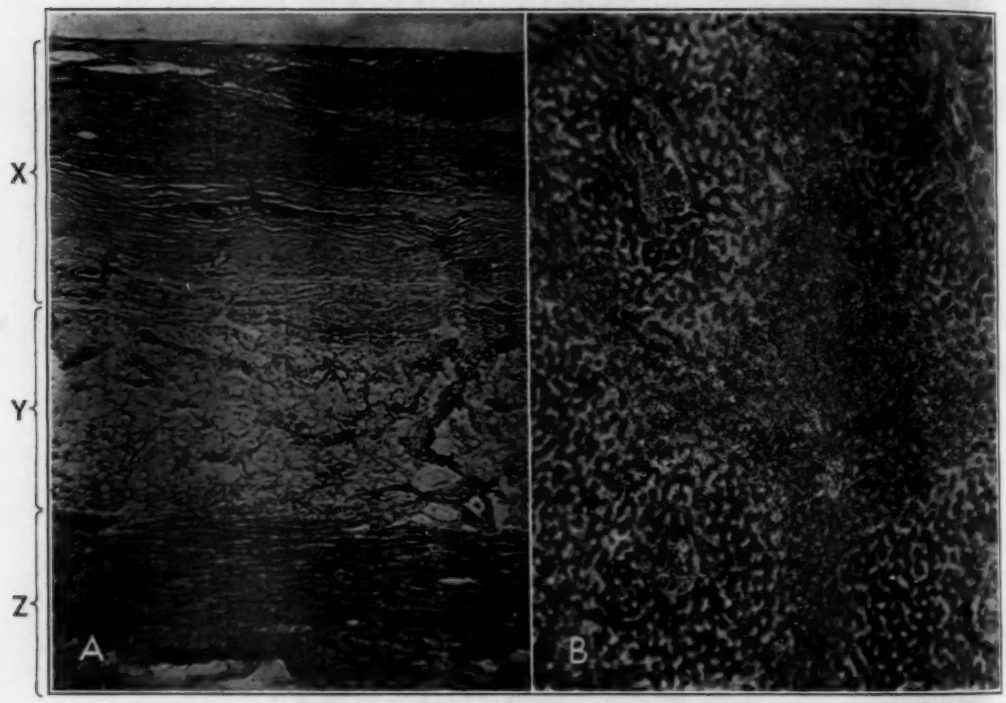

Fig. 7.—*A*, cross-section of epicardium and myocardium; × 43. *X*, thickened epicardium; *Y*, layer of fatty tissue and *Z*, external portion of myocardium. *B*, section of hepatic tissue (× 60), showing dilated sinusoids and necrosis of hepatic cells particularly about the efferent veins. The hepatic cells about the portal systems show the least evidence of damage.

A photomicrograph of a section of tissue from the right ventricle is shown in figure 7 *A*. Sections of the liver (fig. 7 *B*) and spleen showed the changes associated with a severe grade of chronic passive congestion. There was no evidence of tuberculosis in the lungs.

COMMENT

In this case the diagnosis of a thickened, constricting pericardium should have been made much earlier. In a child the history of recurring and persistent formation of ascitic fluid and dependent edema, in the

absence of obvious cardiac disease or of impairment of renal function, is highly suggestive. The low pulse pressure and high venous pressure in the absence of valvular lesions of the heart are significant findings. The electrocardiogram was similar to the one reported by Beck.[3] The complete absence of any visible pulsation of the heart under the fluoroscope is a striking and significant sign. The absence of either visible or palpable pulsation over the precordium in conjunction with the other physical findings points to a markedly thickened pericardium. The cardiac area as determined by the orthodiagram was slightly larger than normal for a child of that age, height and weight. The cardiothoracic ratio in a roentgenogram of the chest taken at a distance of 6 feet (183 cm.) was 0.57, which is at the upper limit of normal.[6] Congestive failure in the presence of a small or normal-sized heart has been mentioned as a diagnostic point in Pick's disease.[4] However, the means at our disposal for determining cardiac area during life do not distinguish between the heart itself and its enveloping membranes. A markedly thickened pericardium and pleura will slightly increase the cardiac area, and thus in advanced Pick's disease the cardiac area may be larger than normal, although the heart itself is of normal size. A shift in the electrical axis with a change from the right to the left lateral recumbent position occurred in this patient. Fixation of the electrical axis with change in the position of the body is therefore an inconstant finding in Pick's disease.

Little additional information on the etiology of the disease is afforded by this case. From the study of a large number of autopsies, Sprague, Burch and White [7] conclude that the condition is probably not rheumatic but results from a tuberculous pericarditis. No evidence of tuberculosis was found at autopsy in this patient. The cervical mass which was incised and drained in childhood may or may not have been tuberculous. No member of the patient's immediate family had tuberculosis. On the other hand, there was no history of rheumatic fever, arthritis or chorea. No Aschoff bodies were found in the myocardium. The edges of the mitral valves were slightly but definitely thickened. The other cardiac valves were entirely normal. As Beck has produced the typical Pick's syndrome by chemical irritation of the pericardium, it is probable that any infection of the pericardium of sufficient severity may result in the disease.

The failure to obtain a cure or marked improvement in this patient after removal of the anterior portion of the pericardium may be ascribed

6. White, P. D.: Heart Disease, New York, The Macmillan Company, 1931.

7. Sprague, H. B.; Burch, H. A., and White, P. D.: Adherent Pericardium and Pick's Syndrome: An Autopsy Study, New England J. Med. **207**:483 (Sept. 15) 1932.

to the presence of a thickened, calcified epicardium. It was thought that the patient's condition after removal of the pericardium did not justify prolonging the operation in order to remove the epicardium. It was planned, if necessary, to expose the heart again at some later date and to remove as much of the epicardium as possible. The feasibility of stripping this membrane from the surface of the ventricles was demonstrated at autopsy. A layer of subepicardial fat separated the thickened epicardium from the coronary vessels and the myocardium (figs. 6 and 7 *A*), so that the epicardium could be separated by blunt dissection, without injuring either the coronary vessels or the cardiac muscle. In one or two places where calcification extended from the epicardium directly into the myocardium, the separation would have been impossible

The condition of the epicardium and the clinical course of this patient were closely similar to those described by Beck [2] in experiment 8 (dog 29-31). Pick's syndrome was produced in this dog by the injection of surgical solution of chlorinated soda into the pericardiac cavity. Resection of the parietal pericardium in two stages resulted in a temporary improvement. The syndrome recurred, however, and the dog died. At autopsy the heart was found encased in a tough, thickened epicardium which, as Beck pointed out, undoubtedly interfered with the normal diastolic filling of the heart, as had the thickened pericardium which had been removed at operation. Beck suggested that such a condition might occur in patients and might necessitate the removal of a portion of the epicardium. It is apparent that in some cases of Pick's disease removal of the pericardium alone is sufficient to produce a dramatic alleviation of symptoms.[8] In the far advanced cases, with a thickened and constricting epicardium, resection of a portion of the epicardium is probably necessary. Schmieden [9] even regarded resection of the epicardium as the essential feature of the operation.

The low values for serum protein observed in this patient two years before operation were subsequently overlooked, and unfortunately the determination was not repeated. The total serum protein, 3.03 per cent, and the serum albumin, 2.14 per cent, were both below the usual level at which edema appears.[10] The reason for the low serum proteins in this case is not clear. There was no albuminuria, and the patient's diet contained an adequate amount of protein. On four occasions the protein content of the ascitic fluid lay between 4.0 and 2.19 Gm. per hundred cubic centimeters. Assuming the protein content of the ascitic

8. Churchill.[1] Beck.[2]

9. Schmieden, V.: The Technique of Cardiolysis, Surg., Gynec. & Obst. **43**:89 (July) 1926.

10. Moore, N. S., and Van Slyke, D. D.: The Relationships Between Plasma Specific Gravity, Plasma Protein Content and Edema in Nephritis, J. Clin. Investigation **8**:337 (April) 1930.

fluid to be 2 per cent, the patient lost approximately 7 Gm. of protein per day by paracentesis in the five weeks prior to the operation. This is comparable to the albuminuria in certain cases of nephritis with edema.[11] However, the low serum proteins found two years before the operation could not be explained on this basis, because comparatively small amounts of ascitic fluid were being lost at that time. The reduction in the serum protein content which frequently occurs in cardiac decompensation suggests the possibility that the long-standing hepatic congestion with its attendant injury to hepatic parenchyma may be responsible for the condition. There is, however, no evidence that either serum albumin or globulin is influenced by hepatic injury.[12] Indeed, Payne and Peters [13] have recently observed that the low serum albumin frequently found in cardiac failure appeared "to be directly referable to malnutrition." As our patient was definitely undernourished, the same explanation may apply. The importance of determining the serum proteins in patients with Pick's disease is obvious. If the protein content is low a second factor is brought into play in the production of the edema and ascites which may well be as potent as the increased venous pressure.

SUMMARY

An anterior partial pericardiectomy was performed on a 12 year old boy with advanced Pick's disease. The thickened calcified epicardium was not removed. There was slight temporary improvement after the operation, but death occurred forty-six days later. At autopsy adhesions were found to have reformed between the heart and the remaining portion of the pericardium. The failure to relieve the patient of his symptoms was attributed to the presence of a thickened epicardium. The significance of the low serum proteins found prior to operation has been discussed.

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11. Linder, G. C.; Lunsgaard, C., and Van Slyke, D. D.: The Concentration of Plasma Proteins in Nephritis, J. Exper. Med. **39**:887 (June) 1924.

12. Peters, J. P.; Eisenman, A. J., and Bulger, H. A.: The Plasma Proteins in Relation to Blood Hydration: I. In Normal Individuals and in Miscellaneous Conditions, J. Clin. Investigation **1**:435 (June) 1925.

13. Payne, S. A., and Peters, J. P.: The Plasma Proteins in Relation to Blood Hydration; Serum Proteins in Heart Disease, J. Clin. Investigation **11**:103 (Jan.) 1932.

TREATMENT OF MYOSITIS, ARTHRITIS AND DISTURBANCES OF THE PERIPHERAL CIRCULATION WITH HISTAMINE BY CATAPHORESIS

DAVID H. KLING, M.D.
LOS ANGELES

Recent investigations have emphasized the significance of disturbances of the peripheral circulation in the etiology of conditions of the joints and muscles. In 1909, Wollenberg,[1] on the basis of arteriosclerotic changes in the affected joints, advanced the theory of the vascular origin of osteo-arthritis; he experimentally produced overgrowth of the patella by a circular ligation of the blood vessels. The experiment was recently repeated and confirmed by Goldhaft [2] and his co-workers, who had previously demonstrated, in studies of the blood flow, blood gases, capillary microscopy and surface temperature, a deficiency of peripheral circulation in arthritis. Hench, Henderson, Rowntree and Adson,[3] of the Mayo Clinic, reported good results in rheumatoid arthritis with ramisection and sympathetic ganglionectomy, which eliminated the vasoconstriction. Von Papp [4] stated that a spasm of the arterioles produces myalgia. The beneficial effect of physical therapy in rheumatic infections is also considered to be due chiefly to a temporary increase of blood supply.

On the basis of extensive studies, Lewis [5] considered histamine-like substances to be the hormone regulating the peripheral circulation. Deutsch [6] therefore conceived the idea of supplying the affected parts with histamine and thus overcoming a possible deficiency. In 1931 he reported favorable results with treatment by galvanic cataphoresis of

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From the Arthritis Department of the Cedars of Lebanon Hospital, Los Angeles.

Read before the Society of Physical Therapy, New York, Feb. 1, 1933.

1. Wollenberg, G. A.: Aetiologie der Arthritis in Lichte des Experiments, Arch. f. orthop. u. Unfall-Chir. **7**:226, 1908-1909.

2. Goldhaft, A. D.; Wright, L. M., and Pemberton, R.: The Production of Hypertrophic Arthritis by Interference with the Blood Supply, Am. J. M. Sc. **180**:386 (Sept.) 1930.

3. Hench, P. S.; Henderson, M. S.; Rowntree, L. G., and Adson, A.: Treatment of Chronic "Infectious" Arthritis by Sympathetic Ganglionectomy and Sympathetic Trunk Resection, J. Lab. & Clin. Med. **15**:1247 (Sept.) 1930.

4. von Papp, quoted by Bettmann.[13]

5. Lewis, T.: The Blood Vessels of the Human Skin and Their Response, London, Shaw & Sons, Ltd., 1917.

6. Deutsch, Dezso: Histamin zur Therapie rheumatischer Erkrankungen, Med. Klin. **27**:1491 (Oct. 9) 1931.

histamine in 250 cases of painful conditions of the muscles. His findings were confirmed by a number of German investigators (Kopits,[7] Trumpp,[8] Friedländer,[9] Payer,[10] Rosenblüth-Ronald,[11] Vas,[12] and Bettmann[13]). Failure with this method was reported only by Ruhmann[14] and Kauffmann.[15]

Through the support of Dr. Jerome Weiss, I was enabled to introduce this method in the Hospital for Joint Diseases.

PHARMACOLOGY OF HISTAMINE

Histamine is, according to Sollmann,[16] a product of the cleavage of proteins by acid, ferments or bacteria. It is found in all tissue extracts and is present in large amounts in the normal stool. But it in turn is rapidly destroyed by bacteria and is therefore not effective when given by mouth. Subcutaneous or intravenous injections of histamine have powerful effects on the circulation and smooth muscles. It is partly responsible for the ergot-like effect on the uterus; it constricts bronchioles and the larger arteries and dilates the arterioles and capillaries. Injections of quantities of more than 1 mg. may therefore cause alarming symptoms, consisting of headache, vomiting, a fall in blood pressure and respiratory disturbances. The theory was advanced that posttraumatic shock is due to liberation of histamine by the damaged tissues.

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7. Kopits, I.: Beiträge zur Definition, Differentialdiagnostik und Therapie "rheumatischer Erkrankungen," Arch. f. orthop. u. Unfall-Chir. **31**:7, 1932.

8. Trumpp, Rolf: Neue Behandlung der Muskelschmerzen, München. med. Wchnschr. **78**:1862 (Oct. 30) 1931.

9. Friedländer, quoted by Deutsch, D.: Zur Behandlung von Schmerzen mit Histamin [Comment on Kauffmann's article], Deutsche med. Wchnschr. **58**:827 (May 20) 1932.

10. Payer, A., quoted by Deutsch.[9]

11. Rosenblüth-Ronald, E.: Die Histamin-Iontophorese und ihre therapeutische Bedeutung, Med. Klin. **28**:1561 (Nov. 4) 1932.

12. Vas, Stefan: Erfahrungen mit der kataphoretischen Histaminbehandlung, Deutsche med. Wchnschr. **58**:1009 (June 24) 1932.

13. Bettmann, Ernst: Neue Wege der Histaminbehandlung schmerzhafter Muskel-, Nerven- und Gelenkerkrankungen, Deutsche med. Wchnschr. **58**:1008, 1932.

14. Ruhmann, Walter: Die örtliche Histamin-Einwirkung bei Muskelrheuma, München. med. Wchnschr. **78**:2201 (Dec. 25) 1931.

15. Kauffmann, M.: Histamine in der Behandlung von Schmerzen, Deutsche med. Wchnschr. **58**:660, 1932.

16. Sollmann, Torald: A Manual of Pharmacology, Philadelphia, W. B. Saunders Company, 1932.

INFLUENCE OF HISTAMINE ON THE PERIPHERAL CIRCULATION

A simple experiment demonstrates the powerful influence of histamine on the peripheral circulation. One drop of a 1:1,000 solution of histamine is placed on the skin, which is subsequently pricked by a sharp needle. Within five minutes an urticarial wheal surrounded by a red flare will develop (fig. 1). The response of the peripheral circulation consists of a triple reaction: (1) a local dilatation and an increase in the blood flow in the minute vessels (purple spot); (2) a local increase in the permeability of the capillaries, which produces the wheal, and (3) a widespread dilatation of the surrounding arterioles (flare).

This reaction [17] was used by Jordan for the diagnosis of the degree and severity of disturbances of the peripheral circulation in Buerger's disease and arteriosclerosis.

Fig. 1.—Stages in the cutaneous reaction of histamine, showing the flare and the wheal.

TECHNIC OF APPLYING HISTAMINE

Cataphoresis.—Deutsch devised for the purpose of cataphoresis a battery galvanic apparatus; he used leaf impregnated with histamine in conjunction with it. The following technic was therefore adopted: A galvanic apparatus equipped with an accurate milliammeter supplies the electric energy. For electrodes, lead foil is used. Blotting paper is moistened with a 1:1,000 aqueous solution of histamine acid phosphate and applied to the affected part. The positive electrode is adjusted over the blotting paper and secured with rubber bandages. Because of the danger of producing burns, care must be taken that the electrode does not touch the bare skin, and all metal should be removed from the vicinity of the current. A convenient negative electrode consists of a nonmetal basin filled with a weak physiologic solution of sodium chloride in which lead foil connected with the negative pole is placed at the bottom of the basin and covered with a rubber sheet. The hand is immersed in the solution. The current is slowly built up to from

17. Starr, I., Jr.: Change in Reaction of Skin to Histamine as Evidence of Deficient Circulation in Lower Extremities, J. A. M. A. **90**:209 (June 30) 1928.

4 to 10 millamperes, about from 1 to 2 millamperes to the square inch of positive electrode being allowed. The current is permitted to act for from one to two minutes.

In the majority of cases no more than a sensation of prickling is felt over the treated part. The current is gradually decreased; contact should not be interrupted suddenly.

By serial connection, with branching cords to the positive pole, a number of parts can be treated simultaneously.

Modification of the Histamine Treatment by Cataphoresis.—An article on this method was recently published by Bettmann.

A nonmetallic (glass, enamel) basin is filled with a 1:10,000 solution of histamine and connected with the positive electrode; it is insulated by a cover of rubber sheeting. The affected extremity is submersed in the histamine. The negative electrode is wrapped in insulating material (linen, towles or rubber) and applied as a cuff over the part to be treated. The current is permitted to act for from five to ten minutes. This method is most convenient in infections of the hands and feet. Drawbacks are the large amounts of fluid necessary and the frequent renewal, as the weak solution deteriorates in from one to three days. The reaction also is not so strong as with the former method.

Scratch Method.—In cases in which a galvanic apparatus was not at hand I have used the following method of application of histamine: The skin is cleansed with gasoline; with a sharp-pointed instrument scratches of about ¼ inch (0.63 cm.) in length are drawn over the affected area in vertical and horizontal directions. The entire area is thus divided into small squares. A piece of gauze is saturated with the 1:1,000 solution of histamine and rubbed into the scratches.

EFFECTS OF THE APPLICATION OF HISTAMINE

I studied the changes taking place in patients and in myself after the application of histamine by these methods.

The exposed skin appeared reddened immediately after the removal of the positive electrode. Soon wheals cropped up (fig. 2) and blended into one patch of urticaria (if cataphoresis was used) or into stripes of urticaria (if the scratch method was used). The temperature over the treated parts rose from 2 to 3 degrees C. (3.6 to 5.4 F.). Gradually the elevation of the skin receded, leaving red spots. The skin returned to its normal appearance in from five to six hours.

Bettmann studied the capillary changes and found a marked increase in the rate of circulation and the number of capillaries visualized and dilatation of the subpapillary vessels. He demonstrated experimentally the marked influence of cataphoresis of a 10 per cent solution of sodium iodide preceded by an application of histamine on the resorption of the skin of rabbits. Controls treated only with iodine by cataphoresis showed, in the section, particles of iodine precipitated with thallium acetate in the superficial layers of the corium, while the sections of the skin which were subject to preceding histamine cataphoresis showed

iodine particles scattered through all the layers. Bettmann claimed also that after prolonged treatment the effect on the capillaries can be demonstrated to last for weeks.

Another evidence of the effect of the histamine on the deep vessels was furnished by Zsedenyi.[18] After ligation of the bleeding vessels in the course of an operation, histamine was applied to the skin adjoining the incision. Thereupon fresh bleeding occurred from the deep small vessels. This permitted an exact hemostasis.

Fig. 2.—Application of histamine by (left figure) the scratch method and by (right figure) cataphoresis.

CHOICE OF METHOD OF APPLICATION

The scratch method has the advantage of simplicity. However, the unequal distribution of the urticaria makes the method less effective than cataphoresis. The lesion of the skin opens the possibility of infection; systemic reaction may occur if the scratches are too deep, and the persistence of the scratches for about a week limits the application of the method.

Cataphoresis, on the other hand, requires an apparatus, but it is the method of choice. It is efficient and does not cause discomfort, and the cutaneous changes are transitory. Systemic reactions were not observed.

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18. Zsedenyi, quoted by Kopits.[7]

The leaf, impregnated with histamine, as devised by Deutsch, offers the advantage of a stable, ready-to-use product, and it obviates the necessity of making up solutions, which deteriorate on standing. The disadvantage, however, is that the leaves come in one size, which is sometimes not sufficiently large to cover the entire affected part. I therefore still use the solutions of histamine on blotting paper cut to fit the required area.

Although I confined myself chiefly to the application of histamine by cataphoresis, the mechanical method has great value, as it proves that the action of histamine is independent of that of the galvanic current.

The problem of iontophoresis and its efficiency is therefore in no wise involved in the histamine therapy of rheumatic infections.

TABLE 1.—*Results of Histamine Therapy*

Diagnosis	Number of Patients	Cure or Improvement		Failure		Recurrence in Total Number of Cases
		Number	Per Cent	Number	Per Cent	
Myositis	376	343	91.2	33	8.8	33 (205)
Static and traumatic myositis	35	32	91.5	3	8.5	
Contractures	29	20	69.0	9	31.0	16
Arthritis	151	124	82.1	27	17.9	22 (81)
Peripheral and circular disturbances	24	20	83.3	4	16.7	
Neuralgias	48	31	64.6	17	35.4	8 (29)
Miscellaneous	67	40	59.7	27	40.3	6 (11)
Totals	730	610	83.5	120	16.5	85 (342)

INDICATIONS AND THERAPEUTIC RESULTS

Table 1 presents a compilation of the collected data on treatment of rheumatic conditions with histamine, which includes 68 cases of my own observation. In a total of 730 cases, 610 patients (83.5 per cent) were either cured or improved; 120 (16.5 per cent) were not benefited. However, in a series of 342 favorable cases, reported by Deutsch and Kopits, Rosenblüth and me,[19] the relief was temporary in only 85 (24.8 per cent).

Myositis (Myalgia).—Three hundred and seventy-six cases, representing about 52 per cent of the total number published, belong to the group of myositis. The prevalence of myositis in the reports to date is explained by the short time that has elapsed since the introduction of

19. Kling, D. H.: Histamine Therapy of Rheumatic Affections and Disturbances of the Peripheral Circulation, Ann. Surg. **99**:568 (April) 1934.

histamine, which permits a definite conclusion only in relatively acute conditions presenting a simple clinical picture.

Table 2 gives a résumé of the results of the various authors and shows that the percentage of cure or improvement lies between 75 and 98 per cent.

An analysis of 32 cases of my own observation is shown in table 3. The ages ranged from 23 to 67 years. Duration of the symptoms amounted to from one week to two years. Previous treatment was given without success in 6 cases and consisted of baking, massage,

TABLE 2.—*Résumé of Histamine Therapy of Myositis*

Author	Number of Cases	Cure or Improvement		Failures		Recurrence	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
Deutsch [6]	94	89	95.7	5	4.3	14	16.7
Trumpp [5]	100	98	98.0	2	2.0		
Kopits [7]	57	56	98.2	1	1.8	12	21.9
Vas [12]	45	40	88.9	5	11.1		
Rosenblüth [13]	48	36	75.0	12	25.0	6	16.6
Kling [10]	32	24	75.0	8	25.0	1	3.1
Totals	376	343	91.2	33	8.8	33	11.2*

* Of 295 cases recorded.

TABLE 3.—*Summary of My Material on the Administration of Histamine by Cataphoresis*

Condition	Number of Cases	Cure or Improvement		No Improvement	
		Number	Per Cent	Number	Per Cent
Myositis	32	24	75.0	8	25.0
Arthritis	24	14	58.3	10	41.7
Subacute bursitis	5	5	100.0		
Tenosynovitis	2	2			
Acroparesthesia	3	2	....	1	
Buerger's disease	1	1			
Angioneurotic edema	1	1			
Total	68	49		19	

diathermy and injections. The muscles of the shoulder were affected in 23 cases; the arm and wrist in 2 cases each, and the forearm, neck, elbow and calf in 1 case each. Cure or improvement was achieved in 24 cases (75 per cent); 8 of the patients (25 per cent) remained unrelieved. No other treatment was given with the histamine therapy. The beneficial results, while lower, show, on the other hand, a smaller percentage of recurrences (3.1 per cent) than do the reports by other authors.

The diagnosis was based on pain, tenderness and limitation of motion due to muscle spasm. Sometimes distinct hardness could be palpated at the insertion in the muscle (myogelosis). In order to exclude pathologic conditions of the bones and joints, roentgenograms were taken in all cases of longer duration which were not readily amenable to treatment.

A thorough examination of all of the muscles of the affected part for pain, tenderness, contraction and nodules is of the utmost importance for success in the treatment. It is a common occurrence, for instance, for a condition to be diagnosed as myositis of the trapezius muscle when further examination would detect tenderness and spasm of the deltoid and pectoralis insertions as well. All affected muscles and the antagonists must be treated.

The effect of the treatment in favorable cases is rather striking. Immediately after the first application, pain and tenderness disappear, and motion is increased. If the initial effect is not pronounced, the final outcome must be viewed with skepticism. This analgesic effect lasts at first for several hours, corresponding to the aforementioned changes in the circulation. The treatment is therefore at first repeated daily, if possible; with the progress of the recovery, the painless intervals increase to twenty-four and forty-eight hours. Treatment is then repeated every second or third day, until all of the symptoms have disappeared. However, I was not able to give the patients at the clinic more than three treatments weekly. The number of treatments required varied from one to seventeen. In severe and chronic cases one is justified in continuing as long as there is a satisfactory and immediate response to the treatment.

Muscular Conditions Following Trauma, Static Strain or Diseases of the Bones and Joints.—Successful treatment of pain and muscle spasm following trauma was reported by several authors in a total of 35 cases, in 32 (81 per cent) of which the patients were cured or improved. This result, if confirmed in a large series, would present decided progress in the after-treatment of injuries to the extremities.

In static myalgia chiefly due to weak feet, Vas reported good results in 25 of 28 cases. In contractures of the muscles, due to pathologic conditions of the bones and joints, Kopits obtained improvement in 29 cases; however, in 16 cases the results were only transitory. Although the treatment in this group was only symptomatic, it could be employed to correct faulty position in preparation for final measures.

Subacromial Bursitis.—In 5 cases of subacromial bursitis, 4 of which showed deposits of calcium in the roentgenograms, I saw disappearance of pain and tenderness and return of complete motion after from four to fourteen treatments. In 3 of the cases previous treatment with diathermy and massage was not successful. If further observation in a large group of cases gives equally good results, cataphoresis should be the method of choice in subacromial bursitis.

I have also had good results in 2 cases of tenosynovitis of the extensor tendons of the hand.

Arthritis.—One hundred and fifty-one cases of different types of arthritic conditions were collected from the literature. Twenty-four cases of my own observation were included. Improvement was noted in 124 cases; the improvement was transient in 22. The results were inconclusive because of the small number of cases and the indefinite

nomenclature used. (Deutsch and Kopits referred to their cases as arthritis deformans and polyarthritis; Vas wrote of "diseases of the joints.")

The analysis of my 24 cases of arthritis is given in table 4. In 14 cases of osteo-arthritis of the knee joint, a diminution or loss of pain and tenderness and a slight increase in motion were seen in 8 cases (57 per cent). Improvement was noted in 2 cases each of infectious and traumatic arthritis and in 1 case of rheumatoid arthritis; in 5 cases of arthritis of the sacro-iliac joint the treatment failed in 4 instances. From this small amount of material I can submit only one conclusion, namely, that there is a difference in the effect according to the type and location of the arthritis; arthritis of the knee joint appears to react far more favorably than that of the sacro-iliac joint.

Neuralgia.—In 42 cases of neuralgia, 31 patients were reported improved; of these 17 were improved only transitorily. Deutsch experienced failure in 3 cases of neuralgia of the cutaneous femoris

TABLE 4.—*Analysis of Histamine in Arthritis*

Type of Arthritis	Number of Cases	Cure or Improvement		No Improvement	
		Number	Per Cent	Number	Per Cent
Osteo-arthritic (knee)	14	8	57.1	6	42.9
Sacro-iliac (joint)	5	1	20.0	4	80.0
Infectious	2	2			
Rheumatoid	1	1			
Traumatic	2	2			
Total	24	14	58.3	10	41.7

lateralis nerve; he regarded histamine as ineffective in pure neuralgia and improvement as an indication that the muscle was chiefly involved, especially in ischialgia.

Acroparesthesia.—Vas reported good results in 18 of 20 cases of acroparesthesia of the hands or feet. I have seen improvement in 2 of 3 cases of acroparesthesia in women of middle age who complained of numbness, hypersensitivity and paresthesias.

Miscellaneous Conditions.—Deutsch had complete failure as to permanent results in 10 cases of painful periostitis. Vas claimed success in 10 cases of furunculosis and in 3 cases of painful infiltrations after perivascular injections. Of considerable greater interest are his good results in a case of Raynaud's disease, in 2 cases of Buerger's disease and in 3 cases of chronic ulcer of the leg. I noticed improvement in 1 case of Buerger's disease and prompt cure after one treatment in 1 case of angioneurotic edema of the knee. The action of histamine in conditions of disturbed peripheral circulation requires extensive investigation.

COMMENT

With the exception of two authors, it is the consensus that the application of histamine by cataphoresis offers an efficient treatment of myositis. The two authors used faulty technic, applying the histamine

to only the painful spots; they neglected to treat the antagonists as well. Neither of the authors published figures of their results. Kauffmann's contention that the analgesic effect is due to the action of the positive pole and not the histamine is without foundation. In order to produce an effect by the galvanic current it is necessary, first, to apply it for a much longer time than one or two minutes and to use a stronger current than is used in applying histamine by cataphoresis. Secondly, the action of the histamine is not dependent on the application by cataphoresis. Its introduction by the scratch method or by intracutaneous, subcutaneous or intramuscular injections showed identical results. Ruhmann conceded to histamine only a counter-irritating effect like that of the application of capsicum. This analogy is only superficial. Both substances produce hyperemia. The diffuse irritation of the skin which is caused by a plaster of capsicum and which prevents repeated application of the plaster, is not produced by histamine, which has a selective action on the blood vessels. The skin returns to normal after several hours, and the histamine can be reapplied immediately.

Ruhmann overlooked further that the action of histamine has been thoroughly investigated and analyzed by scientific methods. Its dosage can be regulated, and its effect can be checked by accurate capillary microscopy, while other counter-irritants used empirically do not permit an accurate investigation.

In arthritis and vascular diseases histamine therapy is still problematic. One does not even know whether the technic used is entirely appropriate. It is possible that a more intensive method of treatment is necessary; I do not see any objection to the application of histamine by cataphoresis two or three times daily for patients in the hospital. Besides being practical, such continuous alteration in the circulation of the blood would be of great importance in the determination of the actual involvement of the peripheral circulation in arthritis. If the treatment is not efficient in itself, it could possibly be combined with other therapy.

SUMMARY

The application of histamine either by cataphoresis or by the scratch method is described.

The effect of this treatment consisted in a dilatation of the minute vessels and the smaller arterioles and in an increase in the flow of blood and in the permeability of the vessels, which caused a hyperemia and elevation of the cutaneous temperature of several hours' duration. Evidence was given of a longer duration of the capillary dilatation after considerable treatment (Bettmann).

The results in 730 cases collected from the literature are surveyed.

A definite conclusion as to the value of this method is at present possible only in myositis. Of 376 patients, 343 were cured or improved; recurrences were noted in 33 patients.

Thirty-two cases of myositis of my own observation are analyzed. In these cases 24 of the patients were cured or improved, and 8 remained unimproved.

Thorough examination and treatment of all of the affected muscles and their antagonists are decisive for the success of the treatment.

Immediate relief of pain and tenderness after the first treatment was of favorable prognostic significance in this group.

Secondary myalgia due to static unbalance after trauma and strain was benefited in a moderate number of the cases reported.

Five patients with subacromial bursitits and 2 with tenosynovitis were successfully treated.

In 151 cases of arthritis reported in the literature, 124 of the patients were improved; in 22 cases the arthritis recurred.

In 24 cases of arthritis of my own observation, 14 of the patients were improved and 10 unimproved.

Long observation of extensive material, however, is necessary to draw definite conclusions as to the effect of the alteration of peripheral circulation by histamine in arthritic and vascular deficiencies.

NOTE.—Dr. Jerome Weiss, director of the department of physical therapy of the Hospital for Joint Diseases, Miss Acton and the staff carried out the treatments.

The patients were derived partly from the orthopedic services of Drs. Finckelstein and Frauenthal, Hospital for Joint Diseases, and partly from private practice.

1930 Wilshire Boulevard.

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.
LOS ANGELES

E. STARR JUDD, M.D.
ROCHESTER, MINN.

JEAN VERBRUGGE, M.D.
ANTWERP, BELGIUM

ALEXANDER B. HEPLER, M.D.
SEATTLE

ROBERT GUTIERREZ, M.D.
NEW YORK

AND

VINCENT J. O'CONOR, M.D.
CHICAGO

KIDNEY

Renal Anomalies.—Nordio [1] reported 2 cases of congenital ectopic pelvic kidney without any associated malformation of the genitals or of other parts of the body. In the first case, during an operation for retroverted uterus, the misplaced kidney was found at the right of the vertebral column and in the pelvic cavity. It was normal in size, without lobulation, slightly flattened and fixed; a fatty capsule was not apparent. As the kidney appeared to be functioning satisfactorily, it was left undisturbed. The patient, a woman who had borne seven children without unusual inconvenience, was seen one year later and was in excellent condition. This case indicates that a pelvic kidney which causes no disturbance or symptoms may go unrecognized throughout life.

The second case, before operation, was thought to be one of unilateral cystic tumor of the left adnexa uteri. As the ureter of the ectopic kidney was too short to permit nephropexy, nephrectomy was done, and the patient was relieved from all symptoms. Owing to the fact that the ectopic kidney was lobulated and embryonal, and, consequently, soft, it presented an almost cystic consistency on palpation, unlike that of a normal kidney.

Kirkland [2] reported a case of congenital absence of one kidney, ureter and suprarenal gland. The remaining kidney was pyonephrotic, an

1. Nordio, Augusto: Contributo allo studio degli errori diagnostici nella distopia renale pelvica in ginecologia, Riv. ital. di ginec. **15**:221 (July) 1933.

2. Kirkland, Keith: Congenital Renal Aplasia, Complicated by Pyonephrosis of the Existing Kidney, M. J. Australia **2**:351 (Sept. 9) 1933.

aberrant renal vein apparently being the obstructive factor. Catheterization of the patient, a woman, aged 36, revealed an empty bladder after anuresis of twenty-two hours. On cystoscopy, the right ureteral orifice could not be found. The catheter could be passed into the left ureter for 20 cm.; urine was not obtained. Operation revealed that the ureteropelvic juncture was sharply kinked by a posterior renal vein coming from the lower pole of the kidney; the lower third of the kidney, which was cystic, was drained. The case is of interest because of the aberrant vessel which made efficient emptying of the left kidney an impossibility, and also because of the large isolated pyonephrotic sac which apparently had been present for a number of years. The patient had successfully gone through three pregnancies with this defective renal system.

Gutierrez [3] stated that at present it is possible to distinguish between, and to identify accurately in advance of operation, three anomalies of the upper portion of the urinary tract which formerly were much confused and frequently were discovered only at necropsy, namely, hypoplastic kidney, renal aplasia and congenital absence of one kidney. The underlying cause of all three conditions is embryonic malformation or lack of proper development of the urinary organs during intra-uterine life, wherein either the kidney does not develop to its full extent or the wolffian duct of the mesonephron fails to produce a renal bud after the duct has reached the cloaca. In view of the fact that congenital anomalies of the kidney constitute about 40 per cent of all pathologic lesions of the organ, the importance of their clinical recognition becomes apparent. The most important points in preoperative diagnosis have been classified on the basis of 8 illustrative cases, in accordance with the principal clinicopathologic and cysto-uropyelographic observations.

The hypoplastic kidney is small or infantile, whereas the other kidney undergoes compensatory hypertrophy. Two types of hypoplastic kidney exist: One contains normally functioning renal parenchyma with both medullary and cortical substance but with diminution in size and deformation of the pelvis, and the other contains no pyramidal or cortical substance, barring a few rudimentary glomeruli and tubules which are visible only microscopically. The pelvis is rudimentary or hydronephrotic in this type, and the calices may be lacking. The ureter is patent in the hypoplastic kidney, urine is normally secreted, and renal function may be normal or diminished; there are also good excretion of urea and elimination of phenolsulphonphthalein. Pyelography and roentgenography reveal a hypoplastic organ. The danger of the finding lies in the fact that such an organ is incapable of undergoing compensatory

3. Gutierrez, Robert: Surgical Aspects of Renal Agenesis, with Special Reference to Hypoplastic Kidney, Renal Aplasia and Congenital Absence of One Kidney, Arch. Surg. **27**:686 (Oct.) 1933.

hypertrophy in the event of surgical removal of the other kidney. Such a kidney is from a sixth to a third the size of its mate, which is always hypertrophic. The chief diagnostic sign is marked decrease in function, both quantitative and qualitative, in comparison with the other kidney, when the latter is normally developed; in the event that the other kidney has undergone pathologic change, clinical evidence alone is misleading, and the necessary differentiation depends also on a correct interpretation of a bilateral pyelogram. If there is an insufficient concentration of opaque substance by the hypoplastic kidney, as shown in the intravenous pyelogram, an ascending pyelogram will be necessary. The differential urographic diagnosis must be borne in mind, since this condition may readily be confused with the lesions observed in secondary renal atrophy acquired through disease. It must also be distinguished from other common types of anomalies, such as double kidney, in which the upper portion of the pelvis alone is diminutive, and one may be misled if the double pelvis and ureters have not both been properly visualized.

Renal aplasia may be regarded as renal hypoplasia of an extreme degree, being distinguished from the latter by the fact that the rudimentary and diminutive structure supposed to be a renal organ is only a small mass of aberrant fibrous tissue which at no time has had any excretory function, although it may be formed, microscopically, of embryonic and sclerotic, or even calcified, glomeruli and tubules. Here again two types exist. In the first, the amorphous mass of renal tissue has a small renal artery coming from the aorta, although there is no evidence of a true renal pedicle, pelvis or ureter; a short rudimentary and functionless ureter, however, may be discovered in the course of a careful postmortem examination. It is thus an organ which has never shown any signs of existence in a true sense and has never accomplished any physiologic function, yet, owing to the presence of an artery, it can eliminate into the mass of tissue the intravenously injected opaque substance, and thus the presence of aberrant renal tissue may be revealed in the urogram. In the second type there is no renal artery but only small aberrant blood vessels anastomosing from the blood supply of the suprarenal gland; thus no shadow results from intravenous injection of the opaque medium. Moreover, although the pelvis and the upper portion of the ureter are absent, there is always evidence of a remnant of the functionless or obliterated ureter in the aplastic side of the urinary bladder. Clinically, the patient has no symptoms related to the urinary tract, the only complaint being pain in the lumbar region. Cystoscopy reveals a normal bladder and two normal ureteral orifices but, on the side of the aplastic kidney, the ureter is found to be a blind stump, after 4, 5 or 6 cm., having no connection with the fatty mass of sclerotic renal tissue; any fluid injected will regurgitate, making only a hypothetic

diagnosis possible. Following intravenous injection of an opaque substance, however, a few tiny patches of shadow may be seen in the roentgenogram where the substance enters the dilatations of the few rudimentary tubules present, which at necropsy will be found to contain a few drops of yellow fluid that may have the characteristics of urine. Histologic section of the specimen removed definitely reveals the presence of renal tissue with embryonic tubules and glomeruli. Areas of calcification or degeneration, to the extent in which cysts are formed, may be seen, as in polycystic kidney. The patients complain of pain on both sides of the abdomen. On the side of the aplastic kidney, the pain is due to remnants of renal tissue which have the irritant action of a foreign body, whereas on the other side, the overwork of the hypertrophied kidney leads to painful symptoms also. Surgical treatment in such cases must be along very conservative lines, consisting in the removal of the remnants of the aplastic kidney with as much of the pararenal fatty capsule as possible.

Like the two preceding anomalies, congenital absence of one kidney has been widely confused with atrophic kidney, fused kidney and also with the two types of malformation already discussed. Once again two types exist: The first is the type of the true solitary kidney, with complete absence of both kidney and ureter on the opposite side. It may be ectopic or in cross ectopic position, but there is only one ureteral orifice into the bladder, and one half of the trigon has not been developed. As a rule, there is some associated genital malformation as well. The second type is the solitary fused kidney, in which there is evidence of union of two nephroblastomas into one organ, with two pelves and two ureters which may open normally or abnormally into the bladder. The solitary single kidney is peculiarly subject to disease, and in the event that it is diseased the prognosis is fatal. The association of a pathologic process, such as parenchymatous nephritis, formation of stones, pyelitis and pyelonephritis, with a tendency toward hydronephrosis, oliguria, infection, anuresis and death, has commonly been recorded in the literature. Through errors in diagnosis, many operations have unwittingly been performed on the solitary single kidney, with fatal results.

The symptoms of these three conditions are insidious. Bilateral pain, with an enlarged palpable mass in one side of the abdomen, may signify hypertrophy of one kidney and demands careful urologic investigation of the upper portion of the urinary tract. Sole reliance should never be placed on the result of an intravenous pyelogram despite the brilliancy of the achievements of this new method, for it cannot be too strongly emphasized that in many cases bilateral retrograde pyelograms are indispensable.

Kemal,[4] writing from Constantinople, reported the case of a man, aged 30, who lived for twenty days with anuresis and practically symptomless uremia after the removal of an infected, calculous right kidney, which proved to be a solitary organ. The importation into Turkey of substances for intravenous use in urography is not permitted and, because of extraneous circumstances, retrograde pyelography also could not be carried out in advance of operation. In this case a stricture of the urethra made the introduction of a cystoscope impossible; therefore, Kemal made only an intramuscular injection of indigo carmine. Since the dye was eliminated after about fifteen minutes, he thought himself justified in concluding that there was a functioning left kidney and in performing nephrectomy. The coralliform shape and great size of the stone revealed at operation would have made its removal by nephrotomy impossible. The kidney, with a widely distended and infected pelvis, was about four times its normal size. On the first day after operation, when the catheter elicited only 10 cc. of a fluid which was mainly pus, the suspicion arose that the kidney which had been removed was solitary. This became a certainty when all measures undertaken to produce diuresis proved ineffectual. The temperature remained normal for five days, however, and the chlorides and the urea in the blood were only moderately increased. Even on the seventeenth day, the patient still felt well enough to inquire when he might be allowed to go home. He was found dead in his bed on the twentieth day, although he had been walking about the room only fifteen minutes before. Necropsy revealed only a barely visible rudiment of a left kidney, in which renal tissue could be seen microscopically. A left ureteral orifice in the bladder could not be found. The distended right ureter was filled only with pus.

[COMPILER'S NOTE.—Solitary single kidney is the condition in which one of the kidneys is definitely absent. The case reported by Kemal is not properly classified, since in the postmortem examination nephrogenic tissue was present as revealed by the naked eye and the histologic section of the mass removed. This case should have been reported as renal aplasia and not congenital absence of one kidney or solitary single kidney.]

Tumors.—Pascual[5] stated that tumors of the renal pelvis are not frequent. Chronic inflammatory processes in the pelvic mucosa of all kinds, leukoplasia and continued irritation set up by a calculus seem to play an important part in the etiology. The chronic inflammatory

4. Kemal, M.: Entfernung einer Solitärniere. Symptomloser Verlauf einer 20 Tage währenden Urämie, Deutsche med. Wchnschr. **59**:1398 (Sept. 8) 1933.

5. Pascual, Salvados: Los tumores de la pelvis renal, Fifth Cong. Internat. Soc. Urol., 1933, p. 82.

factor cannot be a very important one because, if it were, it would be a frequent occurrence to find tumors of the renal pelvis accompany tuberculous processes of the kidney, which is not the case.

Histologically, the majority of tumors of the renal pelvis are of an epithelial nature; these are benign papillomas in some cases and malignant papillary epitheliomas in others. There are also nonpapillary epitheliomas of undoubted malignancy and a few nonepithelial tumors. The relative frequency with which these three types of new growth occur is approximately the same. Nonepithelial malignant growths are extremely rare. Pascual stated that in spite of the fact that it is possible to maintain a histologic distinction between benign and malignant tumors, clinically it is impossible to do so, partly because benign papillomas often degenerate into papillomatous epitheliomas, and partly because these tumors, even the most benign in appearance, owing to their tendency to spread, to metastasize and to generalize, enter into the clinical evolutionary picture of carcinomas and behave just like them.

Pascual stated that the most characteristic feature of tumors of the renal pelvis is their tendency to spread and to propagate within the remainder of the urinary tract, ureters and bladder, where they usually recur and maintain the original histologic type. The manner in which this type of propagation takes place is not definitely known; the mechanism is possibly multiform and may be that of contamination by urinary fluid. Some investigators consider the propagation to be direct, and a smaller group think that the lymphatic system may be responsible. Some also defend the hypothesis of concurrent formation of tumors in the pelvis, ureter and bladder.

Pascual reported that tumors of the renal pelvis present the classic signs of hematuria, increase in volume of the organ and pain (not of frequent occurrence or very characteristic) which generally accompany formation of tumor in the kidney, either in the pelvis or in the parenchyma. From the point of view of symptoms, it is extremely difficult to establish an exact diagnosis as to the situation of the tumor.

Pascual felt that tumors of the renal pelvis are always serious, even in cases of typically benign papilloma, in view of their tendency to propagate, to undergo carcinomatous degeneration and to become transitional forms. The histologically benign nature of the tumors does not exclude the possibility of diffuse metastatic implantation to ureters or bladder, and such metastasis may even be of a malignant nature. The prognosis in these cases is, therefore, serious on all occasions. Pascual concluded that, bearing all these factors in mind, treatment can be only surgical. It should consist of nephrectomy and ureterectomy, either partial or total, according to the surgical possibilities and the condition of the ureter.

Van den Branden [6] stated that there are two classes of tumors of the renal pelvis: epithelial tumors and tumors of mesodermic origin, the latter being extremely rare. Epithelial tumors are divided into three categories according to their pathologic anatomy: papillomas, papillary epitheliomas and sessile tumors. These may be divided into two classes in accordance with their clinical evolution: papillary tumors of a metastatic nature which invade the urinary mucosa and sessile tumors or true carcinomas with local development which penetrate neighboring tissues and are conducive to metastasis. Van den Branden stated that one can never say with absolute certainty that a papilloma is benign, the frequency of its dissemination rendering it dangerous. Nearly every benign papilloma is potentially malignant; although the process is sometimes slow, the development is fatal, death often being due to complications. The principal symptoms are hematuria and pain and a perceptible mass, the first appearing often early in the condition. Hematuria has intermittent characteristics and is likely to appear at any time independent of fatigue or effort. On the whole, it is painless and frequently accompanied by the passage of clots of blood. The mass is not due to the neoplasm proper but rather is the result of hydronephrosis. The increase in volume is more rapid than in renal carcinoma. Pain nearly always appears in the form of renal colic caused by distention of the renal pelvis.

The various types of treatment for this condition are: (1) Fulguration by the urethral route. (2) Resection of the lower portion of the ureter with ureteroneocystostomy. This operation, however, Van den Branden considered inadvisable as it leads to atrophy of the kidney. He suggested that an operation of a more drastic nature is to be preferred. (3) Nephrectomy with partial ureterectomy. With a single incision, that part of the ureter is removed which can be exposed by the usual incision for nephrectomy. This operation is indicated for sessile tumors in the upper part of the ureter or in the renal pelvis. The indication is justified by the fact that these tumors develop by continuity and not by dissemination. Van den Branden reported the following results: patients dying after operation for malignant tumor, 10 per cent; those having recurrence within one year, 64 per cent, and those surviving for more than three years without recurrence, 26 per cent. Of the latter, 3 of 58 had no recurrence in more than six years. In the case of papillomatous tumors, 65 per cent of the patients suffered recurrence in the ureter. Of the 26 patients reexamined, 6 had shown no sign of recurrence in more than three years. (4) Subtotal nephroureterectomy. This operation is performed in one or two stages; in any case, two incisions, one lumbar and one anterior, are made. Van

6. Van den Branden, Fernand: Tumeurs du bassinet et de l'uretère, Fifth Cong. Internat. Soc. Urol., 1933, p. 139.

den Branden stated that it was preferable to leave a minimal interval of time between the two operations. This particular method, however, has not been used very often, the majority of surgeons preferring to complete the operation in one stage and in a more drastic manner. (5) Total nephro-ureterectomy with resection of the ureteral orifice. The frequency of grafts in the intramural part of the ureter indicates its excision. Complete removal complies entirely with all modern and leading principles of surgical treatment of tumor. The postoperative mortality rate is higher (22 per cent), but the final results obtained are of longer duration. An operation in two stages is better sustained, although it is advisable not to allow too long an interval to elapse between operations. Of 10 patients whose cases had been followed, 7 have survived for more than two years, of whom 2 are in perfect health five and a half and seven and a half years, respectively, after operation. The lower part of the ureter is difficult of access, good visibility for operating being difficult to achieve.

Joly [7] stated that epithelial tumors of the renal pelvis are distinctly rare when compared with neoplasms of the kidney itself. Statistics on this point vary greatly, but the average of those available is between 7 and 8 per cent. Epithelial tumors may be divided into two main groups: papillary and the solid growth. Each of these groups has been divided into two subgroups. Thus papillary tumors comprise (1) benign papillomas and (2) papillary carcinomas, whereas solid growths have been classified as (1) transitional cell carcinomas, if they arise from cells similar to those found in normal transitional epithelium, and (2) squamous cell carcinomas, which are formed of cells that have no counterpart in normal transitional epithelium.

Joly stated that papillary tumors are the most numerous, comprising three fourths of the whole series. Of 337 cases which he collected, the tumor was a benign papilloma in 120, a papillary carcinoma in 138, a transitional cell carcinoma in 29 and a squamous cell carcinoma in 50. In more than half the cases of papilloma, the patients were between the ages of 30 and 60, whereas in most of the cases of malignant growth the patients were between the ages of 40 and 70. With papillary tumors, no predisposing causes have been found. These tumors appear to originate in the pelvis of normal kidneys. With solid growths, stone and infection are important etiologic factors. This is most marked with squamous cell growths, more than half of which arise in cases of calculous pyonephrosis. The secondary changes in the kidney usually are due to back pressure; hematonephrosis is formed, with atrophy of the renal parenchyma due to this pressure. Solid tumors have a greater

7. Joly, J. S.: Epithelial Tumors of the Renal Pelvis and Ureter, Fifth Cong. Internat. Soc. Urol., 1933, p. 211.

tendency to invade and replace renal tissue than villose tumors. Pyelography, Joly stated, is the only method by which the diagnosis of neoplasm of the renal pelvis could be definitely established. The symptoms of tumors of the renal pelvis resemble those of renal neoplasm so closely that it is impossible to distinguish them without the aid of a pyelogram. The treatment of villose tumor consists in removal of the kidney and ureter. Simple nephrectomy is so often followed by recurrences in the ureter that it should be abandoned. When the tumor is solid, nephrectomy with removal of the lumbar portion of the ureter usually is sufficient. The prognosis is very grave. A recurrence was found in approximately half of the cases of benign papilloma which were followed, and in about two thirds of the cases of papillary carcinoma. A "cure" has been obtained only rarely when the growth was solid. Tumors of the ureter are much less common than those of the renal pelvis. They are, however, similar in structure, and the same classification has been adopted. In 101 of 133 cases, the growth was papillary. In approximately half the cases, the neoplasm was found in the lower third of the ureter.

Trauma.—Luccioni [8] emphasized the importance of early diagnosis in cases of combined contusions of the spleen and left kidney, in order to make the correct incision with least destruction of the abdominal wall and with a minimum of operative shock. Such an association of lesions increases the seriousness of the prognosis, and in unfavorable cases death ensues rapidly. In Luccioni's case, however, the patient lived until the sixth day despite rupture of the spleen, of the left kidney and of the tail of the pancreas. Goinard reported a mortality rate of 50 per cent in such conditions; Lathuraz-Violet, 66.6 per cent, and Fiolle, 71.4 per cent. Without surgical intervention, the mortality rate is 100 per cent. Diagnosis of the splenic rupture is essential, since this necessitates immediate operation, whereas repair of the renal lesion is less urgent. Signs of internal hemorrhage usually are evident, and the pulse should be watched carefully. There may be violent pain in the left side, although lumbar pain may predominate. The abdominal wall is contracted, especially in the left upper quadrant. Hematuria is marked, usually from the first urination. A perirenal hematoma may be felt on palpation. The condition usually requires immediate surgical intervention too urgent for cystoscopy, urethral catheterization or, even, intravenous pyelography.

There are several different incisions, but the best, as Luccioni stated before, will be that one which, reduced to a minimum for easy cases, can be readily transformed into a wide approach without excessive muti-

8. Luccioni, Francois: Étude de voies d'abord combinées dans les plaies et dans les contusions de la rate et du rein gauche, Arch. d. mal. d. reins **7**:261, 1933.

lation of the abdominal wall. It must give a wide view of the left kidney and of the spleen and expose their pedicles. The main consideration is to accomplish satisfactory hemostasis. Lastly, the incision should not destroy innervation of the abdominal wall and should minimize cutting of muscles. Luccioni has chosen supra-umbilical, median laparotomy, with which there may be combined, in case of need, the horizontal incision of Bazy, the oblique incision of Rio-Branco (upward to the left from the umbilicus), that of Sprengel (downward obliquely to the left from the tip of the sternum), that of Lecene (more vertically upward to the left from the umbilicus) or the dorsolumbar incision of Fiolle. Luccioni preferred Fiolle's incision to the rest because, with no greater destruction of the abdominal wall than with the other incisions, it permits easier splenectomy and nephrectomy as well as inspection of the tail of the pancreas.

Very rarely is conservative treatment of the spleen possible, and partial splenectomy is always hazardous. The renal lesion demands the same treatment as an isolated contusion of the kidney. Total nephrectomy should be done only if the vessels of the pedicle are torn or the parenchyma is crushed into several fragments. If one pole of the kidney is torn apart, partial nephrectomy should be attempted; in other cases, suture, or even tamponade, or these two combined, may be indicated. Drainage of the bed of the spleen will, as a rule, be unnecessary when hemostasis is perfect, but drainage of the renal region will usually be indicated on account of the separation produced by the perirenal hematoma. Fiolle's method has the further advantage of permitting drainage at the lowest gravitational point without supplementary procedures. The incision starts at the axillary line and follows the costal border backward along the lower border of the eleventh and twelfth ribs, encroaching slightly on the lumbar mass. Both the kidney and the spleen are accessible by this route, and it permits extraperitoneal approach to the kidney. It cuts the eleventh and twelfth intercostal nerves, but spares the ninth. It is therefore not destructive and permits ready reconstruction of the abdominal wall.

Stones.—Walters [9] stated that removal of branched stones filling the pelvis and calices of one or both kidneys frequently has been delayed until symptoms of renal infection or obstruction, with partial renal insufficiency, developed. After a decision has been reached as to the advisability of removing such stones, the question arises as to whether to remove them by pelviolithotomy or by a long incision in the convex portion of the kidney, splitting the kidney practically in two portions and thus extracting the stone. Walters reported that his experience with

9. Walters, Waltman: Removal of Branched Stones from the Kidney, Proc. Staff Meet., Mayo Clin. **8**:468 (Aug. 2) 1933.

the latter method has led him to believe that it is impracticable because of the serious bleeding that occurs. Therefore, he has used a combination of pelviolithotomy and nephrolithotomy, retracting the renal parenchyma from the pelvis in order to make a larger incision. He stressed the value of this procedure because, if patients have little extrarenal pelvis, it is impossible to retract the renal parenchyma which overlies the intrarenal portion of the pelvis for a distance of 1 or 1.5 cm. and sometimes more, so that, frequently, the division of the pelvis into its calices cannot be visualized. After as much of the stony material as possible has been removed through the pelvis, and that usually means all but the piece or pieces in the calices, a small opening is made over each calix and the remaining portion of the stone is removed by a combination of pelviolithotomy and nephrolithotomy. Bleeding from openings in the renal parenchyma can be controlled perfectly by the introduction of the Pezzer catheters to be used for temporary drainage.

Bliss, Livermore and Prather [10] studied the relation of vitamins to the formation of calculi. They used rats, which normally are free from urinary calculi; calculi developed in these rats only when they were given deficient diets. The results obtained in this study indicate that an insufficiency of vitamin A in the diet may be a factor in the formation of urinary calculi in rats. In 34 rats of a group of 55 (61.8 per cent) which had been given a diet devoid of vitamins A and D, urinary calculi developed, whereas examination of 32 animals of a group of 56 (57.1 per cent) given a diet devoid of vitamin A revealed stones or sand. From forty to seventy days are required for calculi to form in the urinary bladder of rats. The urinary calculi found during this study were composed mainly of calcium and magnesium phosphates.

Kretschmer [11] reported 3 additional cases of cystinuria and cystine stones. He stated that, except for the complications attendant on the formation of cystine calculi, cystinuria usually is considered a harmless anomaly. It is a well recognized clinical fact that among many persons who have cystinuria for many years, or for a lifetime, calculi may never develop, whereas in others who do not have cystinuria, calculi develop. It is when disease due to a calculus develops that cystinuria becomes of clinical importance.

Kretschmer stated that the question of visibility of the cystine calculus in the roentgenogram is still far from settled. Thus, Holmes and Ruggles stated that the order of visibility of urinary stones is as follows: phosphate and cystine stones, very dense; oxalate stones, next, and urate

10. Bliss, A. R., Jr.; Livermore, G. R., and Prather, E. O., Jr.: The Relation of Vitamin A and Vitamin D to Urinary Calculus Formation, J. Urol. **30**:639 (Dec.) 1933.

11. Kretschmer, H. L.: Cystinuria and Cystin Stones, J. Urol. **30**:403 (Oct.) 1933.

stones, least dense. Harris stated that older reports in which it was stated that cystine stones were not opaque are erroneous, and according to Lewis, the general opinion seems to classify the stones as shadow-casting (often faint). Thomas and Roda are also of the opinion that cystine stones cast a distinct shadow. Hicks said that small cystine stones are only slightly, or not at all, opaque to roentgen rays and, consequently, this means of diagnosis is not important in their detection. It would seem, therefore, that among patients with a history of renal colic whose urine contains crystals of cystine or who give a positive reaction to the test for cystine and a negative roentgenogram, repeated examination with the wax-tipped catheter is in order. Kretschmer stated that the treatment of cystine stones does not differ from that of any other type of stone in the urinary tract, and that most investigators agree that the treatment of choice is surgical. It has been known for a long time that cystine is soluble in an alkaline solution, and the administration of alkalis is recommended, not only to cause disintegration of a stone, but also to prevent the formation of stones in cystinuric persons, or to prevent the recurrence of stones after such patients have been operated on. Because of the tendency of this type of stone to recur, the value of surgical treatment has been questioned, and attempts have been made to produce disintegration of the stone by the internal administration of alkalis.

Walters and Castleton [12] stated that the greatest problem is not surgical removal of cystine calculi, but prevention of their recurrence. Cystine is a complicated organic compound belonging to a group of amino-acids, and is the only compound in this group that contains sulphur. Normally, cystine originates from catabolism of protein, either endogenous or exogenous. Normally, also, there is a trace of cystine in the urine, averaging 4 mg. per hundred cubic centimeters. Crystals are not found normally. In cystinuria, there is usually about three times that amount, and crystals may or may not be present. Cystine may be found in the urine in the form of hexagonal, colorless, highly refractile crystals, or in the form of needles. In alkaline urine, crystals are not found, the cystine remaining in solution. Cystine stones are yellowish and waxy, with a somewhat semitransparent luster. They may be of any size, and cases have been recorded in which the stones weighed 50 Gm. They may be pure cystine, or they may contain admixtures of other urinary constituents. The finding of crystals of cystine in the urine determines the diagnosis of cystinuria. However, as noted previously, cystinuria may be present without the crystals.

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12. Walters, Waltman, and Castleton, K. B.: Cystine Renal Calculus, West. J. Surg. **41**:622 (Nov.) 1933.

Walters and Castleton stated that if crystals of cystine are present in the urine, it does not mean that calculi are present. They stated that many cases are known, especially those of relatives of patients who had cystine stones, in which crystals of cystine had been present in the urine for many years without any evidence of formation of stone. Patients of any age may be affected. They said that there is a difference of opinion concerning the visibility of cystine stones in roentgenograms. In some cases the stones have been shown clearly. Cystine calculi rarely are pure, and, if they contain a considerable amount of calcium, they may cast a clear shadow. In the past, treatment has been discouraging and unsatisfactory owing to the tendency toward recurrence of the calculi. The new dietary control of the urinary reaction will be a great improvement in the future. The first, and usually the simplest, step is removal of the stone. The main problem is prevention of recurrence, and for this purpose a diet low in protein and constant alkalization of the urine have long been recommended.

Tuberculosis.—Lieberthal and Huth [13] stated that the normal kidney does not excrete bacilli of tuberculosis. These bacilli in the separated renal urine always come from the caseous centers of disintegrated tuberculous lesions which are in open communication with the renal pelvis. Tuberculous lesions in the kidney often are accompanied by a variety of secondary nontuberculous degenerative, inflammatory or sclerotic changes. In Lieberthal and Huth's opinion, the inflammatory foci described by various investigators as tuberculous nephritis are secondary nontuberculous inflammatory changes. Bacilluria in these cases unquestionably is caused by undiscovered minute ulcerative tuberculous lesion of the kidney. Nephrosis may develop as the result of pulmonary tuberculosis. The occasional appearance of glomerulonephritis in such cases is due to secondary infection of the tuberculous pulmonary cavities. The bacillus of tuberculosis or its toxins does not produce nephritis.

Lieberthal and Huth stated that in the presence of such an incipient ulcerative tuberculous lesion in the kidney the separated renal urine may not contain pus cells, the kidney may reveal no functional defect, and the bladder may be normal on cystoscopic examination. Such early lesions occasionally may heal and, in the author's opinion, they are responsible for the transient tuberculous bacilluria which sometimes is observed.

Henline [14] reviewed the literature and reported 97 cases in which nephrectomy had been performed for tuberculosis. In 34 cases the original symptoms complained of were: symptoms referable to the blad-

13. Lieberthal, F., and Huth, Theodore: Tuberculous Nephritis and Tuberculous Bacilluria, J. Urol. **30**:153 (Aug.) 1933.

14. Henline, R. B.: Renal Tuberculosis: Diagnosis and Treatment with a Study of 97 Cases of Nephrectomy for Tuberculosis, Surg., Gynec. & Obst. **57**:231 (Aug.) 1933.

der, 85.3 per cent; pain in the kidney, 76 per cent; cloudy urine, 50 per cent; hematuria, 44 per cent, and general symptoms, 35 per cent. Henline stated that the diagnosis is established primarily by pyelographic observations, with evidence of a decrease in renal function in advanced cases. Intravenous urography is a distinct aid in some cases but cannot replace pyelography. Bilateral pyelograms should be made as a routine measure, if the ureters can be catheterized.

Henline said that nephrectomy followed by proper medical treatment offers the only hope of arresting destructive unilateral renal tuberculosis. As much of the ureter should be removed as is possible through the renal wound. Nephrectomy should be performed in those cases in which a destructive lesion in one kidney is manifest with good function of the remaining kidney, that is, when the second kidney can be shown pyelographically to be only slightly, if at all, affected. The operative mortality rate was approximately 3 per cent, and it was highest among young patients. Henline concluded his article by stating that medical care is an essential part of the treatment of renal tuberculosis and should be carried out by one thoroughly familiar with this work.

Seidman [15] cultured 89 tuberculous specimens (81 of which were urine from the bladder or the kidney) from 45 patients; bacilli of tuberculosis were isolated from 60, or 67.4 per cent, of the specimens, and from 39, or 86.6 per cent, of the patients. With 14 of the positive cultures, no acid-fast bacilli had been seen in the direct smear of concentrated sediment. From 14 specimens, in connection with which acid-fast bacilli had been seen in the direct smear, no growth was obtained. Fifteen specimens in which both cultures and direct smear were negative produced tuberculosis in guinea-pigs on inoculation. Seidman stated that a growth of bacilli of tuberculosis was obtained on Corper's crystal violet potato cylinder from 54 per cent of the positive sediments, on Petroff's coagulated egg medium from 69.1 per cent and on Sweany's milk, meat infusion, egg and cream medium from 71.6 per cent. Corper's potato medium is more satisfactory than these results indicate.

In this study, Seidman found that the shortest interval for primary isolation of bacilli of tuberculosis by culture was sixteen days. Growth was obtained within three weeks from 18.3 per cent of the positive specimens, in 7 per cent of the inoculated culture tubes. Inoculation of guinea-pigs still appears to be superior to cultures for the diagnosis of tuberculosis in cases in which the condition is suspected.

Polycystic Disease.—Braasch and Schacht [16] collected data from 193 cases seen at the Mayo Clinic in which the diagnosis had been poly-

15. Seidman, L. R.: Routine Culture of Urine for Tubercle Bacilli, J. Urol. **30**:195 (Aug.) 1933.

16. Braasch, W. F., and Schacht, F. W.: Pathological and Clinical Data Concerning Polycystic Kidney, Surg., Gynec. & Obst. **57**:467 (Oct.) 1933.

cystic kidney. Many of the patients returned for subsequent examination, and it was possible to confirm clinical data previously obtained. In this group were included 85 patients who were operated on for various renal complications occurring with polycystic disease, or who disclosed abnormal renal conditions in the course of operation for other abdominal lesions. Records of necropsy made at the clinic were available in 9 cases, and operative specimens were obtained in 10; therefore, histologic studies were possible in 19 cases. In addition, the observations made at postmortem examination were available in many cases in which death occurred after the patients had returned to their homes. The incidence of congenital polycystic kidney as found at postmortem examination at the Mayo Clinic was 9 in 9,171 cases, or a ratio of 1:1,019. The incidence noted clinically was 193 in 680,000 registrations, or 1:3,523.

Braasch and Schacht stated that the average age of patients at the onset of symptoms was 38.8 years. The average duration of life of patients reported dead had been fifty years. There was definite evidence of a hereditary trend. A systolic blood pressure of 145 mm. of mercury or more was found in 61 per cent of the cases, and the diastolic blood pressure was more than 90 mm. in 55 per cent. Laboratory evidence of renal insufficiency was present in more than 60 per cent of the cases. Surgical complications occurred in approximately 30 per cent.

The most common symptom was dull pain, usually in either renal region. Urinary symptoms of moderate frequency and dysuria often were observed. Gross hematuria occurred in approximately 33 per cent of cases and sometimes simulated that occurring with neoplasm. The first clinical symptoms were frequently those of renal insufficiency, although a remarkable degree of tolerance often was noted in the presence of advanced renal destruction. The prognosis varies largely with the degree of renal dysfunction. If renal function remains normal, the prognosis is good; even moderate reduction of renal function may remain stationary for as many as ten or fifteen years. Expectancy of life will average almost fifty years, although patients frequently are observed who are more than 60 years of age. The hereditary nature of the disease should discourage the bearing of children, and sterilization should be considered.

Meland and Braasch [17] stated that "multilocular cyst of the kidney" refers to a collection of cysts within a cyst. They expressed the belief that such cysts form a separate entity. There were 6 cases classified as instances of multilocular cyst on record at the Mayo Clinic, and they were being reported as examples of true multilocular cyst; 4 other examples were noted from the literature. In 3 cases of multilocular

17. Meland, E. L., and Braasch, W. F.: Multilocular Cysts of the Kidney, J. Urol. **29**:505 (May) 1933.

cysts seen at the clinic, the condition was found incidentally at postmortem examination. None of the patients had had symptoms referable to the urinary tract. In the other 3 cases seen at the clinic, as well as in the 4 included from the literature, operation was performed, and in all cases evidence was present which directed surgical attack on the kidney.

The 6 cases seen at the clinic were reported in detail, and these, together with the reports of the 4 cases in the literature, indicated that the cysts vary in size from 3.5 by 4 cm. to 9 by 10 cm. The number of cystic cavities varied from 3 to 4 to several dozen (in 2 cases). The cavities were separated by complete septums in all three cases. Microscopically, the cysts were identical with solitary serous cysts. The walls of the cysts were composed of compact fibrous tissue in 9 cases. Remnants of renal tubules and glomeruli were present in the walls of the cysts in 4 of the cases seen at the clinic. In 8 of the cases there was a definite epithelial lining, columnar in 3, cuboidal in 2 and flattened in 3. In 2 cases there was no lining epithelium. There was definite evidence of atrophy from pressure in the region adjacent to the cyst in 4 cases. Of the 9 cases in which the kidney was available for study, the renal substance was normal in 5; in 2 there was evidence of chronic slight glomerulonephritis, and in 1 the kidney was normal except for the presence of many small cysts.

Meland and Braasch stated that 2 patients sought medical advice because of a noticeable tumor, and that 2 had pain in the renal region, a palpable tumor being discovered at the time of examination. One patient had had repeated renal colic on the left side and a functionless left kidney; the absence of function was due to an impacted ureteral stone. Meland and Braasch further stated that multilocular cysts and solitary serous cysts have several features in common: Both are unilateral; the walls of the cysts are identical in structure; both involve similar and localized regions of the kidney, and the symptoms of both depend on the size and the situation of the cysts.

Nephropexy.—Mathé [18] reviewed the history of nephropexy, pointing out its popularity at the end of the last century, at which time surgical suspension of the kidney had been perfected to the point that the percentage of failures had been reduced to a minimum. Many surgeons, eager to follow the new fashion, little heeded the criteria for operation advised by sane-thinking urologists, namely, pain, obstructive phenomena, persistent infection and gastro-intestinal symptoms, and they fixed movable kidneys that were causing no symptoms. Others employed methods that did not give lasting fixation. The result was that in many

18. Mathé, C. P.: Nephropexy: Present Day Status and Description of New Technique, Surg., Gynec. & Obst. **57**:538 (Oct.) 1933.

instances operation gave little relief because it had been improperly done and because it had been depended on to relieve renal obstruction that did not exist. This led many surgeons to give up nephropexy, and thus the pendulum swung far and wide to such an extent that the patient in Dietl's crisis, owing to strangulation of a movable kidney, had difficulty in obtaining surgical relief. Mathé pointed out that nephropexy is still held in disrepute by certain surgeons and urologists, who emphasize the failure of this operation in cases in which, as usual, it has been wrongly applied, and who wilfully or blindly fail to recognize its beneficial results in numerous other cases. Many urologists are correctly performing nephropexy. The correct application of this procedure has been due to the development of urography, by means of which renal ptosis, ureteral angulation and changes in the kidney due to back pressure can be demonstrated.

Mathé described a new technic for surgical suspension of the kidney by means of its fibrous capsule, by which a satisfactory high suspension can be achieved and maintained, the height of suspension regulated and lasting fixation assured in a position that will maintain good drainage of urine and relief from symptoms. This consists of taking twenty day triangular chromic catgut sutures in the upper pole, in the middle region or in the junction of the middle region and lower pole, depending on the height of fixation desired. Suspension at a greater height can be obtained by placing these sutures lower in the kidney. The sutures are passed through the musculature above the twelfth, and sometimes the eleventh, rib by means of a Reverdin needle. In this way high fixation of the kidney is obtained, thereby taking up any slack that may exist in the ureter and assuring the straightening of any kinks which may be present. A third, similar triangular suture is taken in the posterior surface of the kidney in the region of the lower pole, and this is anchored to the musculature below the twelfth rib in order to steady the kidney and to prevent torsion or lateral displacement. Mathé emphasized three important steps which are usually necessary for successful nephropexy: ureterolysis, renal sympathectomy and partial decapsulation. Ureterolysis is always performed, by which the upper portion of the ureter is dissected free from the surrounding structures, as a routine measure, in order to eliminate any pressure that may be exerted thereon by aberrant vessels, or a fibrous band, which, left untouched, may defeat the purpose of the operation. Renal sympathectomy is employed only in cases presenting pain. Partial decapsulation is carried out when there is concomitant perinephritis in which the fibrous capsule of the kidney consists of a thickened, indurated, sclerotic shell. Lasting suspension is obtained by removing all fat between the kidney and the posterior and superior walls of the renal fossa and by keeping the patient in bed in the Trendelenburg position for three weeks.

The results obtained from this method in numerous cases were very satisfactory. Routine postoperative pyelographic study demonstrated that the kidney was permanently fixed in a sufficiently high position to free the ureter from kinks, and the results from the employment of this method thus surpassed those of all other methods formerly employed by Mathé.

A New Surgical Technic.—Lowsley and Bishop [19] stated that flat ribbon gut may be used successfully for the purpose of closing wounds in the renal cortex without inserting a needle or suture through the renal substance. A wound in any part of the renal cortex may be repaired by this method. The ribbon gut can be held in the proper situation by means of small loops of fibrous capsule. This method of closing a wound in the renal cortex is an acceptable surgical procedure, because it provides adequate approximation and results in satisfactory anatomic repair of the kidney; it is also compatible with life and health.

Stasis.—Rose and his associates,[20] from an analysis of 385 pyelograms and histories, found evidence that a renal pelvis which generally would be accepted as normal can be so shaped and so related to the parenchyma as to interfere with the free flow of urine, either in the entire pelvis or in a portion thereof. Such a renal pelvis is termed "dysuric." The analysis of pyelograms on the basis of dysuric factors gives functional individuality to all renal pelves and ureters.

Rose and his associates stated that the final importance of such a condition in the pelvis lay in the fact that, in permitting urinary stasis, calculi are formed, infection is incited and continued and idiopathic hematuria and nephralgia may result. The facts given are of value in defining the etiology, in instituting and continuing treatment and in determining the prognosis in renal disease.

Pneumonephrosis.—Mathé and de la Pena [21] reported a case of a rare disorder of the kidney known as pneumonephrosis. It occurred in a case in which the formation of an advanced stricture completely occluded the lower portion of a ureter, resulting in hydro-ureter and hydronephrosis. Infection of the resulting closed sac by colon bacilli resulted in huge distention of the pelvis by pus and gas, entirely destroying the upper portion of the double kidney in which it occurred. The patient presented characteristic symptoms, and the condition was diag-

19. Lowsley, O. S., and Bishop, C. C.: A New Method of Repairing Kidney Wounds, Surg., Gynec. & Obst. **57**:494 (Oct.) 1933.

20. Rose, D. K.; Hamm, W. G.; Moore, S., and Wilson, H. M.: Kidney Pelves; Normal Variations in Their Shape and Flow with Possible Pathologic Significance, Surg., Gynec. & Obst. **57**:1 (July) 1933.

21. Mathé, C. P., and de la Pena, E.: Pneumonephrosis: Report of Case, Urol. & Cutan. Rev. **37**:732 (Oct.) 1933.

nosed by a characteristic roentgenographic picture; the diagnosis was proved by operation, and relief was obtained by a two-stage nephrectomy.

Mathé and de la Pena emphasized and recommended the employment of two-stage nephrectomy for patients weakened and debilitated by the toxic effects of encapsulated renal or perirenal infection. In their case, the first stage, consisting of incision and drainage, permitted the patient to regain his strength and to recover from the effects of toxic and pressure symptoms, thus assuring successful performance of the second stage of the operation, which consisted of extirpation of the diseased kidney.

PERIRENAL ABSCESSES

Vermooten [22] stated that acute suppurative perinephritis (perinephritic abscess) secondary to bacterial (staphylococcic) emboli in the end arteries of the perinephrium is a definite clinical entity and need not have any relation to the kidney, except for the fact that the perinephrium happens to surround that organ. This disease is merely one of the end-results of staphylococcic bacteremia or septicemia. Metastatic staphylococcic abscesses, which develop from staphylococcic emboli, occur not only in the kidney and all the various organs of the body, but they also may and probably do occur in the perinephrium on one or both sides, resulting in acute suppurative perinephritis or perinephritic abscess. The abscess resolves readily with simple incision and drainage. These metastatic abscesses in the kidneys are practically always bilateral. They may occasionally be associated with a similar lesion in the perinephrium, and at times one or more of them may ulcerate through the renal capsule and form a secondary or perinephric abscess.

Vermooten stated that this lesion is a disease of the perinephrium, which is substantiated by the absence of pus cells in the urine in the majority of the cases of staphylococcic perirenal abscesses, the prompt subsidence of symptoms after incision and drainage of the abscesses, the common finding of a normal kidney partly or wholly surrounded by pus at the time of operation and the similar finding at necropsy. Vermooten concluded that this perinephric lesion can be distinguished from a true perinephritic abscess by the presence in a case of the latter type of pus and organisms in the urine, the persistence of these inflammatory products after drainage of a perirenal abscess, the long continued draining sinus or the formation of a urinary sinus after incising and draining one of these abscesses, the presence of calculous or tuberculous disease of the kidney, the occasional finding of a large solitary abscess of the kidney at operation and the common finding of multiple bilateral renal abscesses at necropsy.

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22. Vermooten, V.: The Mechanism of Perinephric and Perinephritic Abscesses, J. Urol. **30**:181 (Aug.) 1933.

URETER

Stone.—Rolando [23] noted that a calculus may remain months or years in a ureter without doing great harm or causing great pain. The tendency today is to limit the operative treatment to as little as possible. Operation by the classic incision is simple, sure, and may often be done quite rapidly.

To establish the position of the stone, Rolando makes a ureterogram with the patient in the Trendelenburg position, and repeats the procedure immediately before operation. He recommends the wearing of a pair of cotton gloves outside of the rubber gloves, since in these cases excessive lubrication constitutes a disadvantage. When the stone is juxtavesical, it can be displaced upward by a finger in the vagina or the rectum. An assistant should be instructed how to do this, as it simplifies and shortens the operation. The incision begins about 4 cm. above the anterosuperior iliac spine and extends mesially to the lateral border of the rectus abdominis muscle, 1 cm. above the crural arch. Section of the muscle begins at the top and continues down to the subperitoneal adipose tissue. The peritoneum is separated, the iliac artery isolated and compressed and the pelvic ureter finally isolated. Two types of cases may present complications: (1) Cases in which the stone is engaged in the juxtavesical segment. Here it is necessary to isolate the ureter until the point where it crosses the vas in the male. A number of small veins may have to be cut. If the stone is not discovered at the moment of operation, the pelvis is explored with the index finger, combined palpation being performed with the surgeon's finger in the small pelvis and the assistant's in the rectum or the vagina. With strong light and well placed retractors, it is easy to isolate the stone, the assistant pushing it up by vagina or rectum. (2) Cases in which the ureter at the level of the stone is sheathed by an indurated mass. It is fortunate that this type is not common for it presents a great difficulty, especially if there is marked periureteritis. To prevent lacerating the large veins, one should operate close to the ureter, but there are cases in which the ureter may not be recognizable in the mass that surrounds and penetrates it; here, it is better to give up the idea of isolating it and to open the canal in the iliac or parietal segment, that is, in the free tract above the mass, and extract the calculus with small stone forceps. Operation should be reserved for stones of 2 cm. or more in diameter; for smaller ones, endoscopic maneuvers are preferable.

[COMPILER'S NOTE.—Ureterolithiasis may present various problems, but, as Rolando stated, in most instances when the stone is smaller than the physiologic lumen of the ureter, it may pass spontaneously or by

23. Rolando, Silvio: Observations sur la lithiase urétérale, J. d'urol. **36**:145 (Aug.) 1933.

cystoscopic maneuvers. In these cases it is desirable to recognize the value of an indwelling ureteral catheter in an effort to secure drainage, relieve infection and further dilate the walls of the ureter, thus assisting the passage of the urinary calculus and preserving renal function.]

Physiology.—Cusani [24] denuded of its adventitia a tract of ureter varying from 1 to 3 cm. in length, in dogs, with a view to getting a better understanding of the physiopathology of hydronephrosis. In nearly every one of his 10 experiments this gradually produced dilatation along the ureter above the tract denuded, which frequently continued up into the renal pelvis and finally, after a lapse of several months, into the calices and even into the renal parenchyma. In a late stage, the solid parts of the kidney tended to disappear progressively through atrophy; the glomeruli formed small cysts, with atrophy of their vascular loops, and the tubules were reduced to cords of epithelial cells or dilated segments which in some places appeared to be similar to true cystic dilatations. In cases like these, when obstruction is not the cause of the phenomena observed, it must be that the ectasia of the tubular apparatus of the kidney and its excretory duct, with all the other changes described, is the result of dystrophic disturbance of the wall comparable to what is recognized as the cause of polycystic kidney. This disturbance is evidently due to interruption of the nerve supply resulting from removal of the adventitia, and it is betrayed in a purely dynamic factor, since the abnormal dilatation evidently leads to marked disequilibrium of the entire hydraulics of the renopyelo-ureteral system, a disequilibrium which, as can readily be seen, may have an injurious effect on the walls of all the glomeruli and tubules. It is to this dynamic factor that Cusani wishes to draw attention as a means of explaining so many clinical disturbances which, although without characteristic signs in their early stages, may culminate in the picture of a renal colic. Recent observations of Blatt, Caporale, Cusani and others seem to demonstrate that peristalsis of the ureter and renal pelvis is regulated by neuroganglionic automotor centers situated in the adventitia of their walls, and that a lesion of these centers gives rise to pyelo-ureteral dilatation through paralysis and atony of the musculature. Such studies constitute a sound experimental basis for the dynamic theory as a means of unifying the physiopathology and pathogenesis of different forms of hydronephrosis. Even in hydronephrosis from calculosis, in addition to an obstructive action, there are grave lesions involving the muscular wall and pyelo-ureteral contractility; in other words, a primary mechanical factor has been supplemented later by a dynamic one. The atony in these cases is never primary but presupposes a profound lesion of the central,

24. Cusani, M.: Sulle alterazioni a tipo idronefrotiche nel rene consecutive alla simpaticectomia periureterale, Ann. ital. di chir. **11**:1032 (Sept. 30) 1932.

peripheral and sympathetic neuromuscular system which may be the result of compression, stretching, inflammation or, as frequently occurs, of infection.

Tumors.—Snyder and Wood [25] reported a case of primary carcinoma of the ureter. The cardinal symptoms of pain and hematuria were present, but there was nothing in the history to distinguish the condition from other, more common urinary disturbances. Catheterization and pyelograms revealed an obstructing lesion low in the right ureter, which, coupled with the physical signs of a mass in the right lower abdominal quadrant, suggested ectopic kidney. They stated that, in view of the condition found at operation and at necropsy, it seemed probable that a successful result might have been expected if the patient had been seen earlier in the disease. Excision of the growth followed by nephrectomy, which was the treatment indicated, could not be carried out because of the poor condition of the patient. Death was primarily due to obstruction of the ureter, which in turn resulted in destruction of the kidney, with accompanying infection, ending in generalized loss of resistance and final overpowering infection. Snyder and Wood stated that ureteral tumors, like vesical tumors, as a rule metastasize late, making early operation with resection of the growth a worth-while objective.

Kirshbaum [26] reported 5 cases of true metastasis to one or both ureters, with the observations made at necropsy. The presence of tumor cells within lymph vessels of the ureteral wall was offered as the criterion of the true metastatic nature of the tumors. The ureter as a site of metastasis is very rare, only 11 cases having been reported in the literature exclusive of Kirshbaum's cases. True metastasis to the ureters should not be confused with invasion of the ureters by extension from such nearby organs as the uterus, prostate gland and urinary bladder when they are primarily involved. One of Kirshbaum's cases indicates that Hodgkin's lymphogranuloma behaves like a malignant tumor. In this case, nearly all the organs, including the ureters, were the site of granulomas which did not differ, in the way of spreading, from the 4 carcinomas.

25. Snyder, W. H., Jr., and Wood, B. S.: Primary Carcinoma of the Ureter, J. Urol. **29**:577 (May) 1933.

26. Kirshbaum, J. D.: Metastatic Tumors of the Ureters, J. Urol. **30**:665 (Dec.) 1933.

(To be concluded)

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